

PRIMARY BRONCHIAL CARCINOMA.

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INTRODUCTION and HISTORICAL SURVEY.

A massive literature on this subject has appeared within recent years, emanating from the Continent, Great Britain and America. While most of the authors discussed the etiological, pathological and clinical aspects of the disease, the majority of papers appear to have been published with the object of focussing attention on the remarkable recent increase in the incidence. They convey the distinct impression that this increase is, moreover, a real one, and not only apparent and to be explained by the improved accessory diagnostic methods, the new pathological conception or case selection, nor by personal or general increased interest due to this recent prominence in medical publications.

If this increase is a real one, as I shall endeavour to show in this thesis, it can readily be understood why Chandler¹⁷ recently said "that if it was so, it was the most terrible menace experienced in this generation." The possible factors in the life of our time which have brought about this condition are of interest and merit discussion. Although formerly regarded as a rare disease, as no doubt it

was, a brief historical review will show that while references to it in older literature are comparatively few, they are not quite so rare as hitherto supposed. The scant notice, however, that this subject receives in the majority of modern text books on Medicine and Pathology is a matter of regret, considering the increased incidence, the recent pathological views, and the advances in treatment; this last being due to perfection and elaboration of technique, a more exact knowledge of Anatomy and Physiology, and, even more important, a fuller knowledge of the pathology. In considering the etiology and pathology, a review of past and current literature will, in as far as is possible, be given, and features in agreement or otherwise with my own experiences, based on a study of fifty-nine cases at the Royal Chest Hospital, London, will be discussed. Of these cases twenty six, that came to postmortem between 1917 and 1928, were included in a series of cases reported on by Schuster,⁹⁶ and are only used by me for statistical purposes, the clinical and pathological study being based on the thirty three cases during the period 1929 to June 1931, and not previously reported on. A further purpose of this thesis is to stress the importance and urgency of early diagnosis, as on it depends the success of treatment in those cases where surgery is applicable; and as it is the only branch

of treatment which can claim actual cures, further improvement may be looked for until in the near future Lobectomy will be the treatment of choice.

The illustrations in the section on Pathology are actual micro-photographs of tumour sections, and have been coloured to represent staining by Haematoxylin and Eosin by Miss McLarty, of the Surgical Research Department, University of Edinburgh.

HISTORICAL SURVEY.

References to neoplasm of the lungs in older medical literature, though often indirect, are nevertheless of great interest. The first I have found is that of Agricola² in the middle of the Sixteenth Century, when he mentions the special form of lung disease from which the miners of the Schneeberg in Saxony so commonly suffered; although he had no definite knowledge of its causation, he suspected that the inhalation of the dust of those particular mines played some part in it. The first publication of pathological importance and interest was that of Morgagni⁸² in 1761, in which he gave a description of his clinical observations and post mortem findings of certain lung cases. One case was that of a man of about sixty years of age, who suffered from blood-stained, purulent sputum, and where after death the

lung was found to be extremely hard, adherent to the pleura and mediastinum, and the seat of a cancerous ulcer. Adler¹ is of opinion that this was really a case of primary bronchial carcinoma. Another case he described was of a woman forty years of age who had a large tumour of the heel and subsequently died of pulmonary disease, and this apparently was a case of metastatic sarcoma of the lungs. There are more cases, also of lung disease, in his work, taken by some authorities to have been cancer of the lung, but the assumption is based on somewhat slender evidence.

Van Swieten¹¹² in 1766 gave his observations on a case of a man fifty years of age, where on post mortem examination the upper portion of the right lung was found scirrhus; this could well have been pulmonary carcinoma, though oesophageal carcinoma was not definitely excluded. It was not until 1810 that cancer of the lungs was definitely recognised as such by Bayle, the favourite physician of Napoleon, who in his "Recherches sur la phtisie pulmonaire" used the term 'phtisie cancerreuse.' These, however, appear to have been cases in which Pulmonary Tuberculosis co-existed with malignant disease. According to Huguenin⁴⁷ it was Laennec⁶² who separated the two conditions, and first showed that malignant neoplasm of the lung was a definite entity by his description of Encysted and Unencysted Medullary Sarcomas.

John Forbes⁶² the translator of Laennec's work into English, mentions that the first British, and probably the first of all observers to draw attention to this condition was John Burns of Glasgow who in 1800 published "A Dissertation on Inflammation" wherein he described such lung tumours under the heading of Spongoid Inflammation. Abernethy in 1809 described similar lung conditions under the title of Medullary Sarcoma in his "Surgical Observations on Tumours," but possibly the best and most comprehensive account at that time is contained in Wadrop's "Observations on Fungus Haematodes or Soft Cancer," published in 1809.

In 1840 Bell of Glasgow drew attention to the clinical syndrome of intrathoracic growths, with an account of the cause of these symptoms and signs due to pressure on adjacent anatomical structures, and founded on post-mortem examinations on such neoplasms. Stokes¹¹⁰ of Dublin corroborated this a few years later, and the cyanotic oedema of the upper thorax and neck due to pressure on, or invasion of the superior Vena Cava, still goes by the name of Stoke's collar. In 1869 Niemeyer⁸⁴ of Tübingen wrote "Cancer of the lung is a rare disease, and primary cancer of this organ is of especially unusual occurrence." Up to this time every intrathoracic tumour, quite apart from its histological character or site of origin was labelled Cancer of the lung, until

Waldeyer¹¹³ demonstrated the true epithelial nature of lung carcinoma. In 1870 Harting and Hesse⁴² published their investigation into the Schneeberg Cancer, and their conclusion, that it was definitely Carcinoma of the lungs, was far from accepted by leading medical opinion of that time, and the disease was still by the majority thought to be Sarcoma or some form of Pneumokoniosis. In 1871 Walshe¹¹⁴ wrote that "Cancer of the lung though very much less rare than was until recently supposed, is still absolutely speaking an uncommon affection." In support he quoted Herrick and Popp who found only six cases of Pulmonary Carcinoma in a series of one thousand and ninety one post mortem examinations.

Walshe published the results of his observations on fifty eight cases of Cancer of the lung, giving a very good clinical picture of the disease and its diagnostic points, but like most observers of his time, his description is that of a late stage.

Roberts⁹¹ in 1873 wrote "Pulmonary Cancer, which is exceedingly rare, is found most commonly at the ages of 40 to 60 years, more males are affected than females, and the large majority of cases are secondary," from which it appears that there were differences of opinion among the medical experts also at that time. An American observer, Austin Flint³³ agreed with the observation of Roberts when he wrote

"Intrathoracic carcinoma is rare, and almost always
 "secondary to carcinoma in other situations."

The clinical and early diagnostic features were apparently neglected, and actual publications on Lung cancer were rare, and even then, most of these dealt only with post-mortem appearances. As late as 1904 Sehrt¹⁰⁰ of Leipzig stated that out of 178 cases investigated, a correct clinical diagnosis of lung cancer was only made in six; this may have been due to the following reasons, firstly practically all literature up to this time had stressed the rarity of the disease; secondly the utterly hopeless prognosis, on account of the complete absence of adequate treatment, did not invite discussion or clinical interest; and lastly accessory examination methods of the utmost diagnostic importance were unknown.

The discovery of the Röntgen Rays in 1895 marked an epoch in the science of medicine; this, after many years of perfecting, especially in the last decade, advanced not only the earlier diagnosis of lung tumours, but also bulks largely in modern methods for its treatment. In 1912 Adler¹ published the clinical and pathological details of several hundred collected cases, and in 1926 Barnard⁶ published his classical paper in which he showed that the so-called small or "oat" celled tumours, previously classed as Sarcomata, were in reality Carcinomata

of bronchial origin; other observers as Maxwell,⁷⁴ Shennan¹⁰³ and Duguid²⁵ corroborated this. It must be pointed out, however, that the earlier writers on this subject described these growths as carcinomatous, and even as late as 1887 Jowers⁵⁴ states that all cases recorded in the medical papers of the time, with one exception, were described as Encephaloid Cancers. It was only in the early part of this century that intrathoracic neoplasms were divided into the two varieties, namely Carcinomata composed of columnar or squamous cells, and Sarcomata, including all the tumours of smaller cells, which was subdivided into Alveolar, Spindle-celled, and Oval-celled.

STATISTICS.

A large proportion of the published work on Bronchial Carcinoma was concerned with the statistical study of the incidence of this disease, and was based on the study of post mortem examinations. Most of these cover a period of fifteen years or more, and show a remarkable increase, not only in the incidence of this disease but also in its relative proportion to all other carcinomata. This increase in most cases dates from the post-war years and still rules today. A few observers, however, have given figures to show that in certain cities or areas, there has been no actual increase in the incidence, though in some cases there was an increase in the relative proportion. There are many difficulties and pitfalls in dealing with masses of figures, collected by different observers with their own particular viewpoints on a subject, and before definite conclusions as to the incidence of a disease are arrived at, careful scrutiny and definite criteria for diagnosis should first be established. Of these according to Rosahn⁹⁴ the following should be absolutely necessary:-

- (1) An autopsy must have been done.
- (2) The carcinomatous nature verified microscopically.
- (3) There must be no reasonable doubt that the neoplasm was a primary growth.

- (4) The percentages should be based on total adult postmortems.

The opponents of the view that there has been an actual increase in the incidence of this disease within recent years, base their arguments along the following lines to prove that the increase is only apparent.

- I. Improved diagnostic methods account for many more cases being diagnosed during life.
- II. The increasing and massive recent literature and the new pathological conception have stimulated clinical interest in the disease.

Other arguments advanced are that increased interest in the disease has led to greater efforts being made to obtain post mortem examinations; also that some of the figures were obtained from special Chest Hospitals, thus giving distorted statistics; and further that with a large, annual fluctuation in the number of postmortems, figures may be obtained giving an apparent increase for nearly any particular disease, so that the political aphorism that "Statistics may be made to prove anything" has also been applied here. I have carefully mentioned all these objections, to show that in every case such figures must be analysed with an unbiassed mind, and agree with the four postulates given. As these statistics are the only means at our disposal to prove the actual and the relative incidence of any disease, I shall attempt to show that the objections mentioned

against the published figures of the incidence of Lung Carcinoma do not deserve to be upheld. Improved diagnostic methods naturally account for more cases being diagnosed, but as all the figures to be used by me are based on postmortem results, and not on clinical diagnosis, this objection can hardly be upheld. The increased interest in this disease may lead to more postmortems being sought and this may affect the figures to a small extent, but it is more likely that autopsies will be sought in cases where the diagnosis before death was uncertain or vague; further it is hardly likely that a small factor like this will make any appreciable difference in the figures of the large, general hospitals, though it may quite conceivably affect those of a specialised Chest Hospital, but figures from such are not included.

There have been no large annual fluctuations in the number of post-mortem examinations in the figures included, and that there can hardly have been selection of cases is proved by the large and steady percentage of all deaths that come to post-mortem in the various large hospitals. The earliest, and perhaps the largest number of reports were of German origin, and I shall examine the Continental Statistics first.

Kikuth⁵⁶ in 1925 published figures from an

investigation into the post-mortems at the Eppendorf Hospital, Hamburg, for the years 1914-23.

	<u>Total post-mortems.</u>	<u>Percentage of Lung Cancer.</u>
1914-1918	10,28344
1919-1923	8,56086

The number of cases of Lung Cancer found post mortem was as follows:-

1889-1899	10 cases.
1900-1911	90 "
1912-1923	146 "

He found a steady increase, not only in the incidence of bronchial carcinoma at post-mortem, but also a rising percentage of such carcinomata to all carcinomatas found; this reached the high figure of 9.5 per cent in 1923, and was second in frequency to Carcinoma of the Stomach.

Dora Hanf⁴¹ published a very excellent paper, and gave figures which she compiled from post-mortem examinations at the Charite Hospital, Berlin.

<u>Years.</u>	<u>Total Autopsies.</u>	<u>Lung Cancer Cases.</u>	<u>Percentage of Autopsies.</u>	<u>Percentage of all Cancers.</u>
1911-1915	6497	37	.56	4.74
1916-1920	6127	37	.6	3.78
1921-1925	6802	87	1.28	7.22

These figures are very illuminating, showing a steady annual number of postmortems averaging 1295,

the actual and relative increase being marked in the period 1921-1925.

Wahl¹¹⁵ gives the percentage of Lung Cancers to the total number of postmortems at the Moabit Hospital, Berlin.

1900-192257 per cent.

1922-1927 1.69 " "

In 1927 they constituted 9.7 per cent of all Carcinomata.

Rau⁸⁹ gives the following figures for the Dresden State Hospital:-

1909-191492 per cent of all postmortems.

1915-1919 1.27 " " " " "

Breckwoldt⁷ giving figures for four yearly periods found that there was actually a decrease in the percentage incidence in the period 1918-1921, though a slight increase for the period 1922-1925 compared to his first group.

		<u>No. of Post-mortems.</u>	<u>Percentage of Lung Cancers to total post-mortems.</u>
1914-1917	3,87846
1918-1921	4,16314
1922-1925	4,38152

Biberfeld¹² gives the following finding in his series of cases:-

		<u>Lung Cancer Cases</u>	<u>Percentage of total P.M's.</u>	<u>Percentage of total Cancers.</u>
1897-1906	..	48	.364	4.8
1907-1916	..	71	.52	6.0
1917-1925	..	88	.72	6.2

⁸⁸
Probst gives figures from Zurich to show the increase, compared only to total Cancers, thus:-

1906-1915 Lung Cancers form 2.23% of all Cancers

1916-1925 " " " 6.64% " " "

De Vries²⁴ gives the following results of a series of post mortem investigations in Holland:-

	<u>Number of</u> <u>Post-mortems.</u>	<u>Percentage of Intrathoracic</u> <u>Cancer.</u>
1910-1913 ... 200015
1914-1917 ... 200040
1918-1921 ... 200045
1922-1925 ... 200095

While showing a low incidence up to 1921 there is a remarkable increase for the period 1922-25.

⁶³
Lavrinovitch published the following figures for Petrograd:-

	<u>Number of Autopsies.</u>	<u>Percentage Lung Cancer</u>
1905-1915	16,047	.38

but the only value of this is to show a comparatively low incidence for the particular period.

In Great Britain some excellent papers have been published giving very accurate statistical comparisons over a long period of years, the first to be published, as far as I know, was that of Herrick and Popp quoted by Walshe, in 1871, in which six cases of pulmonary Carcinoma were found in 1091 post-mortems,

giving a percentage of .55 of the total number of autopsies. In 1903 Rolleston and Trevor⁹³ analysed 3983 post-mortems and found six cases, a percentage of .2. One of the best recent reports is that of Duguid²⁵ who carefully went into the figures for Manchester, and gave the opinion that in that city at all events, a great increase in the actual incidence is taking place.

	<u>Number of</u> <u>Postmortems.</u>	<u>Cases of</u> <u>Lung Cancer.</u>	<u>Percentage of</u> <u>the P.M's.</u>
To end of 1885	2107	...	5
1886-1895	2189	...	31
1896-1905	2174	...	38
1906-1915	2039	...	39
1916-1925	2036	...	51
1926	335	...	11
			3.2

His figures show that the greatest increase took place in the post-War period, though a steady rise was apparent before then. The percentage figures are the highest of any so far published, and raise the question as to what unknown etiological factor is responsible more in Manchester than anywhere else.

Bonser¹³ of Leeds has compiled very careful statistics for that city, and finds that in the period 1891-1927 Lung Cancers have been at the steady figure of round one per cent of all post-mortems, and formed seven per cent of all Carcinomata. 83.6 per

cent of all deaths came to autopsy and although the number of cases of Bronchial Carcinoma rose from eleven in 1914 to thirty three in 1927 and its proportion to total admissions from .112 per cent to .325 per cent, she came to the conclusion that there was no actual increase in the incidence during the last thirty five years, and that there was a decrease in Cancer of the Respiratory Tract, other than lungs.

Simpson¹⁰⁵ gives the figures for London Hospital as follows:-

Percentage Bronch.Carcinoma of
Post-mortems total.

1907-191865
191993
1920	1.07
1921	1.50
1922	1.70
1923	1.82
1924	1.73
1925	2.05

This shows that the incidence in 1925 was four times greater than in 1907.

Percentage Bronchial Carcinoma to
total Cancers on combined Postmortem
and Clinical evidence.

1907-1918	1.8
1919-1925	3.3

He came to the conclusion that this increase is not accompanied by any comparative increase in the total cancers admitted to the hospital, and that the incidence increase is real, and independent of improvement in Clinical diagnosis and pathological outlook.

Maxwell and Nicholson⁷⁵ analysed the figures for St. Bartholomew's Hospital, London,

<u>Total</u> <u>Post-</u> <u>Mortems.</u>	<u>Cases.</u>	<u>Percentage</u> <u>of Post-</u> <u>Mortems.</u>	<u>Total</u> <u>Malig-</u> <u>nant</u> <u>Growths.</u>	<u>Percentage</u> <u>of total</u> <u>Malignant</u> <u>Growths.</u>
1914-1918..2020	11	.54	252	4.37
1919-1923..1992	20	1.0	296	6.76
1924-1928..1851	45	2.43	318	14.15

They found that the period of increase commenced in 1920, and that from then the annual case incidence has been in excess of the average for the whole period, though the total number of post-mortems has been appreciably less. A striking fact is that in the period 1924-28 no less than fourteen per cent of all malignant tumours in the postmortem room of the hospital, took origin within the thoracic cavity.

Shaw Dunn and Powell White¹⁰² prepared composite figures from six of the larger hospitals in Great Britain, and found that the average percentage of Bronchial Carcinoma to the total number of post-mortems had increased from .94 per cent in the period 1903-1907 to 1.69 per cent in the years 1923-27. They give figures for the following Centres.

<u>Total</u> <u>Post-</u> <u>mortems.</u>	<u>Years.</u>	<u>Percentage Intrathoracic</u> <u>Cancer to total</u> <u>Post-mortems.</u>
Birmingham 13592	1903-1927	1.18
Glasgow (Western) ... 5775	" "	1.36
London (Univer-	" "	
sity College) .. 6064		1.45
Edinburgh (Royal		
Infirmery) 10687	" "	1.14

Their report stated "At present all that can be concluded with a fair degree of certainty is the increase in the incidence of primary intrathoracic growths, shown by a large body of figures to have progressed during the past twenty five years."

Playfair and Wakely⁸⁷ showed that the percentage incidence for King's College Hospital in London during the years 1901-1923 was .1 per cent, thus the lowest figure in Great Britain. Shennan¹⁰³ gave the corresponding figure for Aberdeen over the period 1914-1927 as 1.7 per cent.

Peet⁸⁶ gives the following figures for the Royal Victoria Infirmary, Newcastle:-

		Percentage of <u>Post-mortems.</u>	Percentage of <u>all Cancers.</u>
1920-1922	1415	.91	6.8
1923-1925	1461	1.15	8.5
1926-1928	1494	1.81	11.3
1929	429	2.33	14.7

Also showing a rising incidence, but beginning at a later period than in the majority so far published.

As a matter of interest it is worth recording some figures from Chest Hospitals, though as stated they are not to be used as conclusive proof of an increased incidence.

Brompton Hospital, London. (Davidson²¹)

Number of Bronchial Carcinoma
at Post-mortem.

1918-1920	16
1921-1923	15
1924-1926	31
1927-1929	45

At the Royal Chest Hospital, London, the corresponding figures were:-

1917-1922	6 cases
1923-1928	20 "
1929-1931 (June)	33 "

While nearly all American authorities agree that there is an increased incidence of Bronchial Carcinoma in their country, their figures show the disease to be much less prevalent than on the Continent and Great Britain.

Barron⁸ gives the following table of figures for the Minnesota Hospital:-

	<u>Total Post- mortems.</u>	<u>Cases of Bronchial Carcinoma.</u>	<u>Percentage of the Post- mortems.</u>
1899-1911	1333	none	0
1912-1918	2026	4	.2
1919-1921	1003	9	.9

Eloesser²⁷ taking the results of Randolph and Rusk of post-mortems performed at the California

Medical School from 1916 to 1924 finds that Bronchial Carcinoma constitutes 1.3 per cent of the total post-mortems; he considers the increased incidence to be not only apparent, but real.

Wells¹¹⁶ found seventeen cases of Bronchial Carcinoma in four hundred and three post-mortems, but as no comparisons are given, this isolated figure is not of much use.

Grove and Kramer⁴⁰ in a series of 3659 post-mortems covering the years 1917-1924 found that Bronchial Carcinoma constituted .57 per cent of the total post-mortems.

Rosahn⁹⁴ gives the figures for the Boston City Hospital in one of the best contributions to this subject emanating from the United States.

	<u>Total</u> <u>Post-mortems.</u>	<u>Number</u> <u>of Cases.</u>	<u>Percentage</u> <u>of total</u> <u>post-mortems.</u>
1910-1918	964	4	.42
1919-1928	2040	17	.83

He also compiled an interesting table of the total number of reported cases of seventeen authors, showing the increase in the percentage of bronchial Carcinoma cases in the total number of post-mortems from 1899 to 1928, this rise being from .14 to 1.36 and he concludes "that there is an absolute and real "increase of primary bronchial Carcinoma."

Hoffman⁴⁵ An analysis of the U.S.A. Census Office returns shows a steady increase in the number of deaths certified as being due to Bronchial Carcinoma.

In 1914, out of 52,420 deaths from all forms of Cancer, 371 were due to Cancer of the lungs, a proportion of .7 per cent or .6 per cent per 100,000 of population.

In 1924	1586	deaths from Lung Cancer	or at rate of	1.6	per 100,000
1925	1728	" " " " "	1.7	" "	
1926	1892	" " " " "	1.8	" "	
1927	2012	" " " " "	1.9	" "	

The figure for 1924 shows an increase of nearly 300 per cent over that of 1914, and after that there is a steady annual rise.

In a further table comparing the mortality from Lung Cancer in different cities and provinces of the U.S.A. and Canada, a striking feature was the figures for New Orleans for the years 1919-1923, in which the death-rate for Europeans from Lung Cancer was 2.8 per 100,000, while that for the Coloured population was .6 per 100,000.

Weller¹¹⁷ gives the percentage of Bronchial Carcinoma in successive thousands of post-mortems at Michigan as follows:-

<u>Number of post-mortems.</u>	<u>Percentage of Lung Carcinoma.</u>
1 - 1000	.1
1001 - 2000	.5
2001 - 2450	.8

¹⁴
Boyd says "When all allowances are made we are forced to the conclusion that the increase is widespread and real."

From a consideration of all these statistics it is clearly seen that the great majority of observers note an increase, not only in the actual incidence of bronchial carcinoma, but also in the relative proportion of lung cancers to all cancers; while the incidence of cancer in general at the present day, according to figures lately given by Dr Dunlop, Registrar General for Scotland, show no real increase. It is true that the majority of neoplasms formerly labelled Mediastinal Sarcoma are now included under Bronchial Carcinoma, and this it can be argued, will affect some of the figures quoted; but then those observers who used the term Intrathoracic Cancer or neoplasm also showed a marked increased incidence. The figures given by Simpson, Maxwell, Weller and many others were all substantiated by the microscopical examination of sections of all the cases as far back as twenty years and more. Melville⁸¹ mentions "that for twenty years I have never missed the

"opportunity of seeing every post-mortem examination
"at the Brompton Hospital, and I am quite certain
"that the morbid anatomist of twenty years ago would
"not have passed over the cases, which are now being
"seen once or twice every week, had they been present
then."

Thus though it is quite conceivable that some
clinicians of that time may have missed the malignant
character of this lung disease owing to lack of
accessory diagnostic methods, it is hardly likely
that the pathologists at all the large hospitals for
which figures are given, who were very able men and
under whom the majority of lungs showing suspicious
conditions would have been sectioned and examined,
would not have noted malignant disease had it been
present.

Simpson in his Analysis of all the bronchial
Carcinoma cases that came to post-mortem at the London
Hospital since 1907, claims that only fifty three per
cent were clinically diagnosed during life; if this
was generally correct even to a lesser extent, we may
assume that many deaths from lung diseases outside
hospitals, which do not as a rule come to post-mortem
examination, must have been due to Bronchial Carcinoma.

ETIOLOGY.

Sex.

In my series of fifty nine cases forty nine were males and ten females, giving a ratio of nearly five to one; this preponderance of males is the finding of most observers. Bonser¹³ found a ratio of 3.5 to 1, Maxwell, Wahl¹¹⁵ and McCrae¹²⁰ 4 to 1, Schuster 3 to 1, Rist and Rolland⁹⁰ 3 to 1. Marchesani⁷³ in a series of 13,367 cases found the sexes equally affected. Lubarsch⁶⁸ in a series of 86,261 autopsies collected from all Germany found that Carcinoma of the lung comprise 8 per cent of all cancers in men, and only 2.57 per cent of all cases in women. In my own series the high ratio is possibly due to the small number of cases investigated. In 1897 West¹¹⁸ found the ratio 3 to 1, and thus, whatever the cause of the increased incidence since then, it is evidently one which affects both sexes in practically the same ratio today.

Age.

In my series the age incidence was as follows:

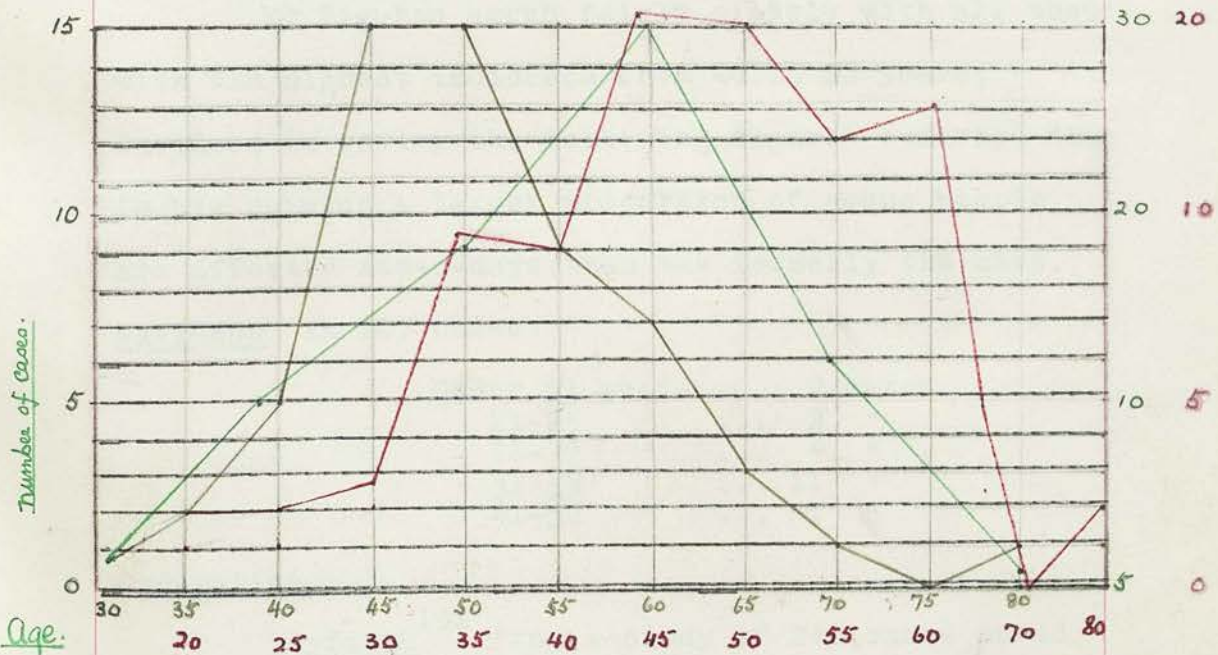
26 - 30 years	1 case
31 - 35	" 2 cases
36 - 40	" 5 "

41 - 45	15 cases
46 - 50	15 "
51 - 55	9 "
56 - 60	7 "
61 - 65	3 "
66 - 70	1 case
71 - 75	0
76 - 80	1 case.

Average age - 51.1 years.

When the age incidence is corrected for the constantly declining population of aged people, it will probably be found that it agrees closely with the age incidence of Carcinoma in general.

Curves illustrating the Age Incidence.



Green represents the figures of HOLZER.

Red represents the figures of DAVIDSON.

Black represents my series of cases.

Kikuth's series:-

20-29 years ... 7 cases.
 30-39 " ... 18 "
 40-49 " ... 49 "
 50-59 " ... 77 "
 60-69 " .. 60 "
 70-79 " .. 30 "
 80 and over .. 5 "

Holzer's⁴⁶ series:-

20-29 years ... 1 case.
 30-39 " ... 10 cases
 40-49 " ... 18 "
 50-59 " ... 30 "
 60-69 " ... 12 "
 70-80 " ... 5 "

Duguid in 173 cases had at age under 21 5 cases
 21-25 .. 9 "
 26-30 .. 6 "
 31-35 .. 11 "
 41-50 .. 60 "

Bonser found the highest age period from 40 to 60 years, this period accounting for 68 out of 178 cases. Maxwell and Nicholson also found similarly, having 64 in this age period out of 100 cases.

My figures agree fairly closely with all these with the highest incidence from 40 to 50 years, Davidson in giving the following figures remarked that in his opinion a larger proportion of young people are affected now-a-days than was formerly the case.

Davidson in 107 cases:

Under 21 years ... 2 cases
 21-25 " ... 2 "
 26-30 " ... 4 "
 31-35 " ... 11 "
 41-50 " ... 41 "

Occupation.

Seyfarth¹⁰¹ from a study of 246 cases noted that Pulmonary Carcinoma was almost exclusively a

disease of labourers and manual workers, occurring with special frequency among tobacco workers, metal workers, type-setters and printers. Marchesani agreed with this but added cases of coal-miners, sandstone workers and Felters.

Duguid states that in Manchester the disease occurred equally amongst indoor and outdoor workers, but as 75 per cent of the adult population of that city is engaged in indoor work, he concludes that it is more likely to affect those whose occupations are mainly in the open air and especially so among transport workers, the inference being that the inhalation over a prolonged period of dust and chemical impurities in the atmosphere may play some part in the causation of the disease. Maxwell and Nicholson found in their cases that 66 had indoor and 34 outdoor occupations. In my cases 38 were engaged in indoor and 21 in outdoor occupations. It is a matter of great difficulty and uncertainty to draw any conclusions from the high incidence among any class of workers in a certain locality, as a correspondingly high proportion of the working population of such an area may be employed in a specialised branch of labour peculiar to that locality, for example Transport workers in Manchester, Coal miners in Durham and Steel workers in Sheffield.

It is noteworthy that most of the recorded cases, and all in my series, belonged to the so-called "Working Class," but as they form the mass of hospital class cases, and as the professional class seldom if ever come to post-mortem examination, it is difficult to know whether the factors pre-disposing or causal in this disease affect one stratum of society more than the other. The only occupation which can be definitely held to play a part in the production of bronchial Carcinoma is the mining for certain metallic ores at the Schneeberg in Saxony; and this being the case it merits a full discussion.

In 1410 mining for Copper was first begun there, and ninety years later the frequency of lung illness in the miners was commented on. At different periods arsenic and cobalt were also extracted from these mines, but at the present day cobalt alone is produced. Koelsch⁵⁹ states that between 1879 and 1915 there were 140 deaths from pulmonary cancer, and of 124 invalided miners 52 were clinically diagnosed as suffering from bronchial cancer. Rostoski, Saupe and Schmorl⁹⁵ after long investigation found that 70 per cent of the workers there, who developed Pneumokoniosis, subsequently, contracted lung cancer after a period varying from five to twenty years. Arnstein³ reported that nearly one-third of all the miners in this district admitted to hospital in the years 1907

to 1911 was with a diagnosis of pulmonary cancer. More recently 154 cases were investigated by the Saxon Cancer Committee, the majority of these were found to have suffered from cough with haemoptysis for many years, possibly due to Pneumokoniosis. Bronchial Carcinoma was diagnosed after examination in 21 of these cases, and in thirteen of these who died the post-mortem confirmed this. In all these cases only a very few gave evidence of Tuberculosis. The high incidence of lung Cancer among the miners was in marked contrast to the rest of the population of that district in whom pulmonary cancer was a rare occurrence, The reason for the high percentage of Bronchial Carcinoma in these miners, in contrast to the low Carcinoma but relatively high Pulmonary tuberculosis incidence in the Witwatersrand gold miners, may be explained possibly by the difference in the irritant. In South Africa the gold ore or "Banket" consists of a quartz conglomerate, the dust inhaled being pure silica; in Saxony the ore contains Bismuth, Cobalt and Arsenic, and in addition is radio-active. Carcinoma of the lung as a complication of Silicosis was only found in two cases during the years 1924-1926,¹⁰⁸ apart from Silicosis it was found in five cases in Johannesburg during this period. In 1930 at the Johannesburg General Hospital¹⁰⁹ there were four cases of Bronchial Carcinoma out of 371 post-mortems. The

possibility of Arsenic being a factor in the Schneeberg must be considered, as Jonathan Hutchinson⁵⁰ drew attention to the fact that the prolonged oral administration of this drug, even in moderate doses, may be followed by Skin Carcinoma.

The possible inhalation of various fungi which grow in profusion in the mines has recently been cited as a factor. In view of the work of Fibiger,³² who produced gastric carcinoma in rats by feeding them on Spiroptera infected foods, this theory must be given some consideration. Observations made in the Skuterud mines in Scandinavia, the Dobschau mines in Czecho-Slovakia, and the mines of Cobalt City in Canada, where conditions analogous to the Schneeberg were stated to be present, have not revealed any increase in the incidence of Bronchial Carcinoma in the miners in these districts, - this shows that there is some unknown agent present in the Schneeberg not found in other similar mines. If we accept mechanical, chemical and fungus irritants as definite factors in the etiology of Schneeberg carcinoma and apply this to the non-occupational forms of the disease, we must assume that certain irritants are now present in the atmosphere which were absent or present only in negligible quantities previous to this increased incidence noticed within recent years.

Rostoski, Saupe and Schmorl recorded two cases of miners who had worked for more than ten years in the Schneeberg mine and had then left the district, taking up other occupations; both of them developed bronchial carcinoma, the one fifteen years and the other twenty two years after having left. It would thus appear that the incubation period of cancer may be very long, probably varying between five and twenty five years.

Inhalation Irritation.

Joannovic⁵³ says "The constant inhalation of "finely-divided vegetable dust appears to be cause of cancer in the Respiratory Tract in Cattle, Sheep and horses. The remarkable increase of bronchial Carcinoma in man has been variously ascribed to Metaplastic epithelial proliferation secondary to Influenza, War gassing, and the abuse of tobacco. Upon the grounds of various observations one is more and more inclined to attribute to the inhalation of dust and the resulting Pneumokoniosis a greater significance in the origin of pulmonary Cancer." Some writers think that workers in a dusty atmosphere, as in Potteries, Building trades, metal and road workers, are specially liable to this disease. Apart from these specific occupations, the great majority of the population spend their leisure in the open air, and such possible factors as inhalation of tar fumes, dust from tarred

roads now almost universal, and the fumes of petrol and oil from the enormous and ever increasing motor traffic, must be considered. It is well known, both clinically and experimentally, that cancer of the skin may follow prolonged irritation with tar. Kimura⁵⁷ produced lung cancer in rabbits and guinea-pigs by insufflating tar fumes through a tracheotomy wound. Moller⁸⁰ painted the backs of rats with tar, and in six of these he found, not cancer of the skin as expected, but carcinoma of the lungs. Thus it can easily be understood that the modern tarred roads may be a factor, as also the exhaust fumes of motor vehicles, though there is as yet no reliable or strong evidence for its acceptance, on account of the difficulty in investigating it statistically or assessing it experimentally or clinically.

The right bronchus is slightly shorter and wider than the left in the proportion of 10 to 7, and it takes a more vertical course towards its hilum, it follows therefore that there is a greater tendency for dust and other foreign, irritating, inhaled material to enter the right lung, and so it should be more affected by this disease than the left. Adler suggested this, but found no marked disproportion between the two lungs in his investigation, nor did Kikuth and Marchesani, but Duguid, Barron, Simpson and others

found the right lung more frequently involved. In my cases the right lung was the seat in twenty eight cases, the left in twenty four and seven were indeterminate. As, however, the minute dust particles concerned are very freely disseminated as a rule, it can hardly make much difference in its effect on the two lungs. Davison²² asserts that chronic irritation is the principal causal factor, citing the inhalation of coal dust, gases and tobacco smoke. The latency of irritation factors has been mentioned.

Poison Gas.

It was suggested by Kraus⁶⁰ that the increased incidence since the War may possibly be due to so many soldiers exposed to poison gas returning to civilian life, the preponderance of males being mentioned as being significant. Huguenin, and also Probst⁸⁸ considered this, but concluded that there was no evidence of it being a causative factor in the cases seen by them. Maxwell and Nicholson found a history of "Gassed in the War" in four of their hundred cases. Brockbank¹⁵ reports four in his sixty two cases, Schuster had three such cases, and one worker in irritating gas. In my series there were four with such a history. I do not think it must be too lightly dismissed as a factor, in view of the fact that Chronic Bronchitis is almost a constant after-effect in these

cases, showing that some pathological changes have occurred in the Bronchi, while in others with no symptoms the irritation may be present though latent.

Influenza.

On the statistical side great stress has been laid on the fact that the increased incidence of bronchial Carcinoma appears to coincide with Influenza pandemics. Benda⁹ and Kikuth have shown that lung Carcinoma increased after the outbreak of 1889. Barron, Fried³⁴ and Moise⁷⁹ in the U.S.A. all point to an increased incidence since 1918. On the Continent Berblinger¹⁰ and Sonnenfeld¹⁰⁶ show a marked increase following this Influenza epidemic. Ferenczy and Matolsey³⁰ also attribute importance to the fact that the greatest increase in the incidence in Vienna was in 1924 and that since then it has decreased. Seyfarth reveals a similar condition in Leipzig. Staehelin,¹⁰⁹ however, notes that the sharp increase in Basel started in 1912. In this country Maxwell and Nicholson and Simpson found an increased incidence, starting in 1919 and 1920 respectively, while Duguid is frankly sceptical as to the relationship between the two diseases. A further argument in favour of it being a factor is the frequency with which such a history is given by patients with bronchial Carcinoma. Grove and Kramer⁴⁰ and also Lenk⁶⁵ drew attention to

it, and more recently Wahl and Loewy-Lenz⁶⁴ emphasised this. Against it is the well known fact that Influenza covers a multitude of symptoms in the lay mind, and is the most common of all self-diagnosed illnesses; also none of the observers in this country, except Davidson with 20 per cent, noticed any frequency of such histories, Maxwell only in seven cases, Simpson in five out of 139, and in my series in five. A third point cited in its favour, is the claim of many observers that the pathological changes in the lungs in Influenza favour the development of Carcinoma. During 1918 Askanazy⁴ noticed regenerative metaplasia resembling precancerous epithelial proliferation in the bronchial mucous membrane in thirty-eight cases, and Teutschlander,¹¹¹ Siegmund¹⁰⁴ and Marchesani all drew special attention to such proliferation being most active in the basal layer of cells, in fact the first named described what he called "basal cell tumuli," These changes agree largely with the post-inflammatory precancerous condition described by Krompecher.⁶¹ Mackenzie⁷⁸ and Haythorn⁴³ noted very similar changes after Pneumonia. These pathological findings must not, however, be accepted as dogmatic evidence, for though strong evidence of some irritative factor on the bronchial mucous membrane, they have possibly only attained

their great importance by the coincidence of the pandemic with the increased incidence of lung cancer, and by the frequency of an influenzal history in conjunction with this disease noted by some observers. Kerley (cit. Schuster) states that though Iceland suffered more than any other community during the 1918 epidemic, bronchial carcinoma is unknown there. A further objection is the contrast between the two conditions in respect to sex incidence.

Tuberculosis.

Ewing²⁸ makes the striking statement that Pulmonary Tuberculosis is the most common etiological factor in the origin of Bronchial Carcinoma; in support he mentions the frequency with which Carcinoma develops in the healed scar of Lupus Vulgaris.

Letuelle⁶⁶ reports two cases of Primary Bronchial Carcinoma developing in the vicinity of active tubercular lung lesions. This connection between the two diseases is, however, much disputed. Morris and Landes⁸³ report no instance of Bronchial Cancer in 662 cases of Pulmonary Tuberculosis at post-mortem. Kikuth does not believe it is an etiological factor, though he found evidence of Tuberculosis in twenty-two out of 246 cases. Adler, as Ferenszy and Matolszy, show very few cases of concurrent Tuberculosis.

Cherry¹⁸ expresses the view that Carcinoma attacks in later life those who had overcome Tuberculosis at an

earlier age, and considers that Tuberculosis is a predisposing factor to Cancer, in that the body cells react in a different way to the same stimulus, the bacillus Tuberculosis. He points out that the combined death rate for Cancer and Tuberculosis vary very little over the last thirty years, constituting approximately 20 per cent of all deaths after the age of twenty five years. I have already remarked on the curious fact that Pulmonary Tuberculosis is common in combination with Silicosis in South Africa and Carcinoma very rare, while Carcinoma is common in the Schneeberg and Tuberculosis rare. It is well known that old, healed Tubercular lesions are found in the lungs of about 90 per cent of the White race, and though it is not impossible that malignant disease, when it occurs in the lung primarily, may light up an old focus of Tubercle, it must be a very rare occurrence. The death rate and incidence of Pulmonary Tuberculosis in all civilised countries is diminishing, while that of Bronchial Carcinoma is increasing. I am not convinced that Tuberculosis of the lung is of any etiological significance except in so far as it is a chronic inflammatory disease.

Syphilis.

Schmoller⁹⁸ suggested this as a possible etiological factor, but very few instances in all the

thousands of reported cases are mentioned. That the two diseases rarely co-exist is not disputed.

Trauma.

Maxwell cites Aufrecht⁵ who considered severe trauma to have been an important immediate precursor to Bronchial Carcinoma in four of his cases. Similar observations have been made by Georgi³⁵ and others. If the large number of cases reported on within recent years are considered, and the practically complete absence of such histories, it forces the conclusion that the trauma may have made a special impression on the patient, or may have been mere coincidence.

Intrinsic Predisposition.

Weller¹¹⁷ is of opinion that this is not sufficiently noted by the mass of writers, and that it is worth fuller investigation; he quotes in support of his view the experimental work of Slye, Tyzzer, and Lynch, which proved the importance of hereditary factors in the formation of tumours in mice.

A family history of a positive character is often obtained during the examination of patients suffering from pulmonary Carcinoma; in my own series a definite history was given in twelve cases; but the predominance of a negative history, the unreliability of many personal and family histories, and the difficulty of applying experimental selective breeding

experiments in animals to man, make such a factor too vague and inconclusive.

Summary.

1. All possible etiological factors are discussed without bias, and no one factor is found to explain the causation nor the increased incidence.

2. A combination of various factors mainly irritative - Mechanical, Chemical, Bacterial, Fungoid or Radio-active - may be responsible. Whatever they are, they have in common the ability to incite hyperplasia and metaplasia of certain cells; males are more affected than females; they are more active or in greater concentration within the last fifteen years.

3. The only certain occupational factor is in the Schneeberg Miners' Bronchial Carcinoma, probably due to some inhaled irritant or irritants, the exact nature of which is unknown.

PATHOLOGY.

The pathology of Bronchial Carcinoma, no less than its other aspects, has also been the subject of numerous investigations since Barnard called attention to the epithelial nature of the numerous Intrathoracic Lymphosarcomas previously reported, and in view of this new pathological conception named them the "oat-celled Carcinomata." Before proceeding with a description of the macroscopic appearances of these tumours, I shall give brief quotations from various contributors on this subject, illustrating their views on the naked eye characteristics and nature of Bronchial Carcinomas.

Barnard says "The obvious Carcinomas other than Squamous, usually consist of a mass surrounding a bronchus of the first or second degree, often near the hilum; the Squamous type is inclined to be massive and to replace the greater part of a lobe or lobes. The oat-celled variety as a rule forms a large mass in the Mediastinum, and a smaller mass surrounding a bronchus of the first to third degree near the hilum; isolated nodules in the opposite lung are more apt to occur." Bonser commenting on a

series of 28 obvious Carcinomas and 24 oat-celled, remarks "No very definite opinion as to the nature of the tumour can be arrived at from the naked-eye appearances. It is significant that in neither type does one hear of the hilum of the opposite side being involved, especially if, as was formerly assumed, the tumour originated in the mediastinal lymph glands."

Schuster states "There is no relation between the type of growth and the size of the mediastinal mass" in fifty four cases investigated by her.

Simpson "Bronchial Carcinomas are really more often than not indistinguishable, but the oat-celled type tends to be softer, more often and more extensively necrosed, invades the mediastinum more often, compared to the obvious type which is firmer, more definitely acinar, and the main mass in close relation to a bronchus. But no reliance must be placed on these distinctions."

Maxwell divides all these tumours according to their mode of spread and infiltration into four types, first where the primary tumour remains localised at its site of origin, secondly where it infiltrates the lung, thirdly where it infiltrates the mediastinum, and lastly where it involves both of these adjacent structures. In his 184 cases, 8.2 per cent belonged to the first, 26.6 to the second, 19.6 to the third and 45.6 to the last type.

Taking for granted that there is no naked-eye difference in the appearance of the different varieties of Bronchial Carcinoma, it appears that the best classification, from a view of the gross pathology, is into three types according to the site of origin and the manner of spread - namely Hilar, Nodular and Diffuse. The so-called primary Miliary Carcinoma of certain publishers is most likely a metastatic miliary neoplasm with an undiscovered primary focus. A case described by Lorey⁶⁷ illustrates this well. The patient during life was diagnosed as a case of acute Miliary Tuberculosis. On post-mortem the lung condition was indistinguishable from Miliary Tuberculosis, but a small carcinoma was found eroding the pulmonary artery, and the cancerous nature of the small nodules or tubercles was only discovered on microscopic examination; Lorey described this as a case of true Miliary Carcinoma.

The Hilar type forms the large majority, arising usually at or near the bifurcation in a main bronchus. Another frequent site, according to Kikuth, is in the main bronchus near the opening of the first lobar branch, the appearance from the lumen ranges from a roughness of the mucosa or a narrowing of the lumen through polypoid masses to complete stenosis, this latter being the most common condition on post-mortem. It infiltrates around and along the bronchial

tree, radiating into the alveolar substance and the mediastinum. It is yellowish-white in colour, firm in consistency except where there is necrosis, which, when extensive, may give rise to cavitation.

The Nodular type, developing in the substance of a lobe is much less common (see Case 2.). ⁹⁵Schmorl described a few such cases from the Schneeberg. When the nodules are multiple there would be a strong suspicion that they are secondary to cancer elsewhere, or multiple metastasis from a small primary pulmonary neoplasm, though Gray and Cordonnier³⁹ from a study of post-mortem cases of very early Carcinomas of the lung, gave very definite evidence to show that multiple nodular carcinomas of the lung may arise from multiple origins, as well as from early metastases. The lobar situation does not exclude bronchial origin, as will be shown when the Alveolar type of Carcinoma is discussed. In this variety secondary infective complications are rare, though Pleurisy is common.

The Diffuse type is a rarity, showing rapid and massive infiltration with widespread destruction of lung tissue, either of a whole lobe or the major part of the whole lung. The mediastinum is often invaded, and there is seldom Stenosis of a large bronchus. Huguenin, Pissavy and Blanche⁴⁹ published quite a few such cases, and Kirklin and Patterson⁵⁸ think that this type is more common in America than is generally thought.

True Mucin formation is occasionally seen in any of these types, but is most common in those of cylindrical cell origin (see Case I.). The Mucin may be found in the alveolar spaces or may be retained in droplet form with neoplastic cells of the "Signet-ring" variety. A type of "Lymphangitis Carcinomatosa" has been described in which a small, discreet tumour in a large bronchus, impossible to detect clinically or radiologically, invades the glands near the thoracic duct and by compression and invasion of this duct causes flooding of the pulmonary lymphatics with malignant cells, also giving the appearance of acute Miliary Tuberculosis.

Microscopic Appearances.

"All agree that there is great diversity of "cell-type and development, not only in different tumours, but also in different parts of the same tumour, and it is therefore necessary in classifying these "tumours to study several sections from the same case. "In the oat-celled variety an alveolar arrangement of "cells in at least part of the growth is readily demonstrable." This quotation from Bonser sums up the general opinion. Passler⁸⁵ as far back as 1896, observed that in the majority of cases, Pulmonary neoplasm can be shown to have its origin in the bronchial system, and that no conclusive proof existed of carcinoma arising from alveolar tissue proper. Kikuth,

Barron and others classify these growths as arising

- i. from Columnar epithelium lining the bronchi
- ii. from the Mucous glands of the bronchi,
- iii. from flattened alveolar epithelium

The polymorphism of cells so characteristic of these neoplasms renders such a clear-cut division impossible in the majority. Simpson says that in the obvious type there may be columnar, mucous, cubical, polyganal, spherical and squamous cells, or a combination of these with intermediate form cells; while the oat-celled are distinguished by oval cells with deeply staining nuclei, and in many of them small areas with definite epithelial characteristics, or in which the cells take up a definite epithelial arrangement. He came to the conclusion that a definite classification on microscopic appearances was difficult on account of the numerous elements composing the lung, the great variability in cell structure in the same and in different tumours, and lack of knowledge of the exact origin of the oat-celled type. When it is considered that the lining epithelium of the bronchi is continuous with the epithelium of the mucous glands and with that of the alvioli, it can readily be understood that tumours arising in any of these three are bound to show considerable overlapping. Schuster divided her fifteen obvious cases into Columnar, Polymorphic and

Spindle-celled types. The oat-celled she described as having gradations from cubical to round and oval cells, "some have fine trabecular scaffolding with loosely arranged cells in rows or rounded spaces; the cells may be oval, cubical or small columnar in shape; Others have thick strands of connective tissue bounding spaces filled with oval or round cells with no definite arrangement and often with necrotic areas; giant cells, single or multinucleate and mitotic figures may be seen, there are numerous blood vessels but they have no intimate connection with the malignant cells as in Sarcomata; they usually show their epithelial origin in the secondary deposits."

Alveolar Carcinoma.

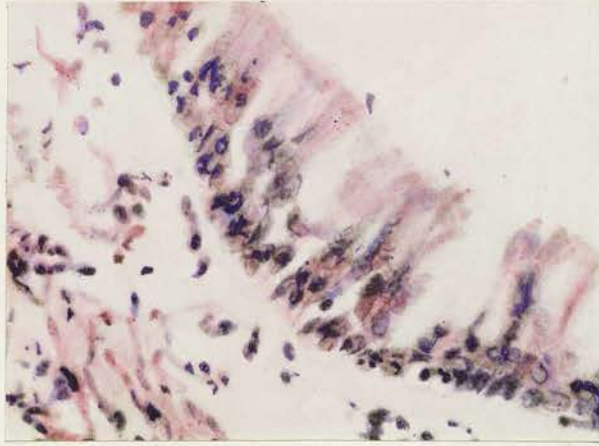
Huguenin states that "Numerous authors think that the Alveoli are capable of giving origin to malignant tumours more particularly of a small-celled type," and Adler holds that "A Carcinoma of the lung tissue itself occurs, but is extremely rare, and built up not of flat, but of cylindrical epithelial cells." Gordon³⁷ described certain cases cystic in type, and some again resembling the Grey hepatisation stage of Pneumonia, while others looked like Colloid Carcinoma; they varied greatly in malignancy and in no case was there Bronchial infiltration. A diagnosis of Alveolar Carcinoma may have been made by some based on the anatomical position, or possibly it may have

been secondary to aspiration from a small, primary bronchial growth. Normally the lining membrane cells of the alveoli are attenuated and often not even recognised microscopically; under inflammatory conditions, however, there may be a proliferation of round cells, while in chronic conditions, as Bronchiectasis, there may be a lining of cubical cells, and in Pneumokoniosis it has the power of extruding phagocytic or "Dust" cells. This adaptibility of the Alveolar membrane may have led some observers to believe that Carcinoma may arise in them, but no positive evidence has up to now, been produced in support.

Barnard commenting on the microscopical appearances, noted that in the obvious Carcinomas there was usually great variation in the histological picture of the cells, and that in some, oval cells indistinguishable from the "oat" cell type, were present; while in the "oat-celled" Carcinomas the cells were mainly oval, with oval, deep-staining nuclei containing very little Cytoplasm, and were arranged mostly in solid acinar manner. Cells other than "oat" were found in nearly all sections, and in some the oat cells were grouped as if attempting to form tubules.

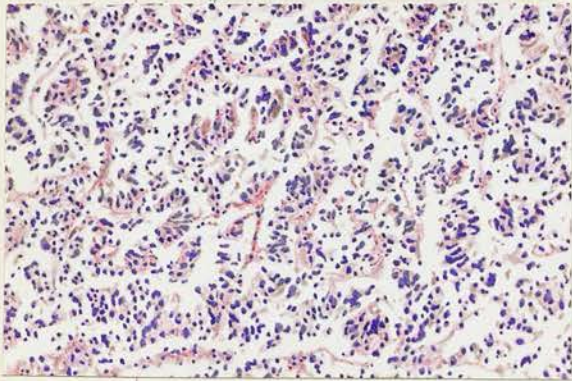
Obvious Bronchial Carcinoma constituted thirty four of my cases, or 57 per cent. In the majority of cases the structure was more or less that of a mucus-

Fig. I.



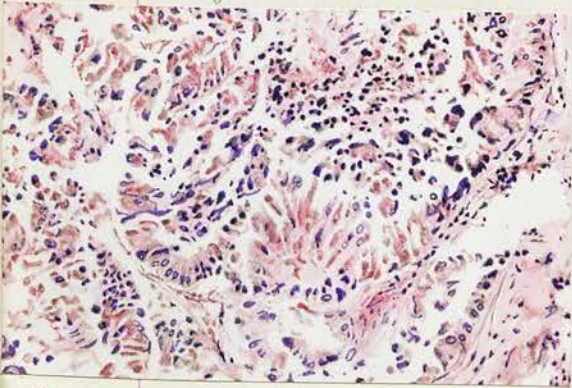
Normal Bronchial mucosa, showing columnar ciliated epithelial cells and a basal layer of transitional cells, some being of 'oat' shape.

Fig. II.



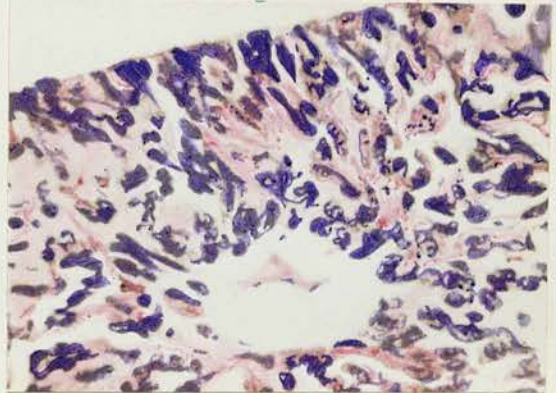
Small or 'oat' celled Carcinoma with fine fibrous trabeculae and loose arrangement.

Fig. IV.



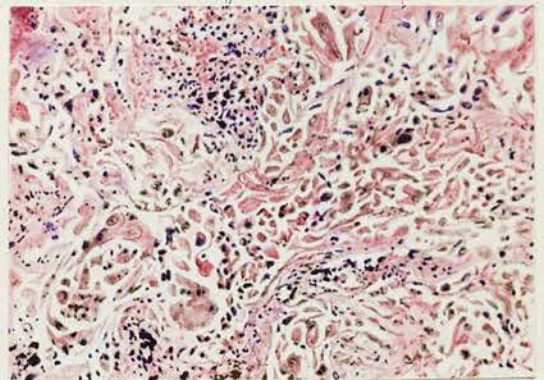
Obvious 'columnar cell type' Carcinoma. Variation in shape & size of cells - some with deeply staining nuclei and oat shaped.

Fig. III.



'Oat' celled tumour (high magnif.) showing deeply staining nuclei and little cytoplasm of cells - cells at edge of cuboidal and columnar shape.

Fig. V.



Obvious 'squamous cell type' carcinoma showing numerous cells with deeply staining nucleus and of oat shape.

secreting columnar cell Carcinoma, though there was considerable variation in individual tumours in the form of cell type varying from high columnar to low cubical, such ranges often occurring in the same growth. In some tumours there was in addition a small number of cells polygonal or oval in shape, and quite like the "oat-cell" of the formerly labelled "Lymphosarcoma" (see fig.4). In others again the structure was that of a frank Squamous celled Carcinoma consisting of prickle cells with an occasional attempt at cell-nest formation and keratinisation; in other parts the growth was mainly of columnar cells, but in this type too, some small round and oval cells with deeply staining nuclei were seen, usually at the periphery of the Squamous cell strands (see fig. 5).

Origin of these Tumours.

The bronchial tube is normally lined by columnar epithelium, and the development of a Squamous-celled Carcinoma in such a situation calls for explanation, and this may be found in the embryology. In the embryo the primitive lung bud develops as an outgrowth from a groove in the floor of the primitive pharynx and is lined by stratified epithelium; later in the development the lining cells become columnar, thus the Columnar form is not necessarily stable and the potentiality to revert to a stratified form is ever present. This is shown by the fact that in both

children and adults localised Squamous Metaplasia of the bronchial epithelium occurs in conditions of chronic irritation, e.g. in Tuberculosis, Influenzal and other Pneumonias; and in the chapter on Etiology authorities for this are quoted.

There is no reason to doubt that a similar reaction can take place in neoplasms. Without assuming developmental errors such as cell-nests of Squamous epithelium, it is even possible that in cases of primary Bronchial Carcinoma prolonged irritation or chronic inflammation may start the squamous metaplasia before actual tumour formation develops. Wolbach and Howe¹¹⁹ have shown experimentally in rats and guinea-pigs, that subtle nutritional changes in the body, such as caused by a diet deficient in Vitamin A, may effect widespread transformation of columnar epithelium into Squamous in the bronchial mucous membrane.

Oat-celled Carcinoma constituted twenty-five, or 43 per cent, of my cases.

These consist of anastomosing strands of small oval, darkly staining cells with a relatively large nucleus and a thin layer of cytoplasm. These cells resemble oat grains and only appear round when cut transversely. In the majority there was very little intercellular substance and the cells often lay in direct contact with each other, a characteristic more

of Carcinoma than of Sarcoma (see Fig.2). The blood vessels were as a rule well formed and were not in that intimate relation to the neoplastic cells as usually seen in Sarcoma. Frequently a tumour consisted of cells ranging from the predominant oat through spingle-shaped or polygonal to ill-defined cuboidal or columnar (see Fig.3) and every grade of transition between these extremes; on occasions these spindle or transitional cells were arranged as if to form a lumen, also a characteristic rather of Carcinoma.

Previous to Barnard's publication it was generally accepted that the neoplasm under discussion arose primarily from the lymph nodes or connective tissue of the mediastinum, but more so from the former as the name Lymphosarcoma implied. The great difficulty in accepting this view is that the tumour bears no resemblance to primary neoplasms of the lymph nodes or connective tissues in other parts of the body. The two primary neoplasms of lymph nodes recognised at the present time are Lymphosarcoma consisting largely of lymphocytic cells, and the Reticulum cell Sarcoma derived from Reticulo-Endothelial cells, but the structure of these is quite unlike the so-called Mediastinal Lymphosarcoma. Though Barnard produced convincing evidence of the carcinomatous nature of this "oat-celled" tumour, it is clear that its structure differs greatly from the obvious Bronchial Carci-

noma, arising from the columnar cells of the bronchial mucosa, and it is difficult to conceive that the oat cell tumour can arise directly from the same type of cell. The explanation given by Maxwell is, in my opinion, eminently satisfactory and well-founded. He emphasises, as did Teutschlander and others before, that the columnar epithelium of the bronchial tree from the trachea down to microscopic bronchioles, does not lie directly on the basement membrane, but is separated from it by a layer of rounded or oval cells, darkly staining and in contact with the membrane (see Fig.1). Some of these cells enlarge, become spindle-shaped and pushing off from the basal membrane, pass in between the bases of the superficial columnar cells; eventually these may reach the surface and presumably by assuming the columnar form replace the normal loss of surface epithelium. There is a very striking similarity in structure between these basal cells of the normal mucosa, and the various forms of cells in the "oat" tumour, and the conclusion that the oat-celled carcinoma takes origin from these cells appears justified. Admittedly, the oat-celled tumour, although carcinomatous in nature, is a distinctive neoplasm, and in the majority of reports of collected cases appears to have a greater incidence than the obvious type. The only other extensive mucosa surface lined



by columnar epithelium is the Intestinal tract, and Maxwell very naturally asks why such tumours do not arise there, and answers this question by pointing to the difference in anatomical structure, in that in the Intestinal tract "the Columnar epithelium lies directly upon a basal membrane with no interposition of a deeper layer of smaller parent cells." Here and there, however, in the Jejunum and Ileum, there are islands of such cells, lying beneath the columnar cells, and it is significant that these cells, which owing to their affinity for silver stains are known as Argentaffine cells, are most common in the Appendix. The researches of Masson⁷⁷ have shown that the so-called "Carcinoid" tumour of the Intestine is derived from these Argentaffine cells, and though this type of neoplasm is very rare it is a curious fact that it most commonly occurs in the appendix. It would thus appear that the frequency of basal tumours in the bronchi, and its rarity in the Intestine, can be correlated with the extent and number of basal cells present in the respective mucosae.

Pathological Complications.

The neoplasm itself may undergo patchy necrosis, hemorrhage may occur into it, and areas may break down, and with secondary infection give pus formation and abscess cavities. In the lung consolidation of a

lobar type was found post-mortem in six cases, and of a Broncho-pneumonic type in seventeen cases, Lung abscess in eight cases, the majority in bronchiectatic cavities, and gangrene was found in one. Partial or complete occlusion of a large bronchus occurred in just over 50 per cent, and in the majority of these Bronchiectasis and areas of consolidation were present. In four cases there was post-mortem evidence of active Tuberculosis, and in a small number healed processes and scarring were seen. In four cases with a positive Wassermann reaction during life, no evidence of syphilitic lesions of the lung were found at autopsy.

Simpson noted that the Secondary Bronchiectasis of Bronchial Carcinoma never, in his experience, gave rise to Cerebral Abscess, and this was confirmed in this series of cases. Pleural effusion was found post-mortem in nineteen cases; in ten of these it was clear and in nine hemorrhagic; Epyema was present in four. Apart from these, old pleuritic adhesions were present in twenty two cases. Maxwell observes that "dense old adhesions" were present in the majority of his cases, apparently older than the neoplasm and in only 25 per cent of these there was macroscopic infiltration; in view of the limited movement of the adherent lung, he considers that it may have some bearing on the etiology, in that the inhaled irritants would be more concentrated in the affected lung, and so

determine the initial point of malignant change. The Pericardium was directly invaded in a number of cases, and in one there was a purulent effusion. Thrombosis of the large veins was noticed in three cases, and the Superior Vena Cava showed either direct infiltration or some obstruction by surrounding growth in ten cases.

Metastases.

Apart from the regional glands, and the frequency of metastases in the extra-thoracic glands, as the Cervical, Clavicular and Axillary, I was impressed by the numerous cases in which the Abdominal glands were affected, this occurring in ten cases. Blood-born metastases occurred in over 50 per cent of the series in the following order of frequency:-

Liver (20),	Suprarenals (14),	Pancreas (5)
Thyroid (3),	Brain (3),	Stomach (3)
Intestines & Omentum (2)	Spleen (1)	Kidney (1)
	and Femur (1)	

Of these only twelve were clinically detected during life. The bones and brain were not systematically examined for these, unless there were indications for such during life.

SUMMARY.

1. Macroscopically the various types of primary Bronchial Carcinoma are very much alike; and

with some exceptions, can only be differentiated according to their site of origin or mode of spread.

2. There is no relation between the type of growth and the amount of mediastinal infiltration.

3. The formation of Mucin does not necessarily prove that the Carcinoma takes origin from the bronchial mucus glands; the character of the mucosa with its different elements and the variability of cell structure in the same tumour, makes differentiation difficult.

4. Microscopically and histogenetically primary Carcinoma of the lung is of bronchial origin; the alveolar origin is found not proven.

5. The histogenesis of the "Obvious type" as following metaplasia is accepted.

6. Support is given to Barnard's verdict that the former "Lymphosarcoma" or oat-celled type, is carcinomatous in nature and structure, and the argument is advanced that these neoplasms take origin from the oval basal cells of the bronchial mucosa.

7. The pathological complications commonly found at Autopsy are mentioned, as they occurred in this series of fifty nine cases.

SYMPTOMS and PHYSICAL SIGNS.

Analysis of main Symptoms and Signs.

Onset was sudden and acute in ten cases, in three the disease was diagnosed as Acute Pleurisy, in two as Haemoptysis of unknown cause, in another it began as an acute, sudden pain in the retrosternal region and was diagnosed as Angina, in one other as Empyema following Pneumonia, one as a Cerebral Thrombosis, and the other two as a Lobar Pneumonia and Acute Laryngitis respectively; in the last named the initial symptom was Hoarseness soon followed by Aphonia and dysphagia. In the other forty nine cases the onset was insidious and gradual.

It is a difficult matter for various reasons to give a typical, clear and concise clinical picture of Bronchial Carcinoma, and there is a possibility that by insisting on the necessity for conciseness and clarity it may preclude this disease from being portrayed in other than a fully developed form, and at a stage where opportunity for any but symptomatic treatment has long passed. When this neoplasm has reached the stage of obvious symptoms and physical signs, it is usually complicated by secondary conditions in the lungs due to infection, or to metastases

in the thoracic cavity or further afield. Though in most cases with an acute onset, the symptoms point to the Chest as being their source, in a few the localised growth in the lung may be small and quiescent, and attention focussed on some dramatic, sudden condition, as a Hemiplegia due to cerebral Metastasis.

I have arranged the symptoms and signs in the order of frequency with which they occurred in my cases as follows:-

1. Cough was the prominent or main complaint in 50 cases						
2. Dyspnoea	"	"	"	"	"	42 "
3. Sputum was present					"	40 "
4. Haemoptysis	"	"	"	"	"	38 "
5. Pyrexia	"				"	38 "
6. Wasting of some degree					"	35 "
7. Pain					"	33 "
8. Dilated veins	"				"	14 "
9. Night Sweats	"				"	11 "
10. Cyanosis	"				"	11 "
11. Oedema	"				"	8 "
12. Dysphagia	"				"	7 "
13. Laryngeal paralysis					"	6 "
14. Finger clubbing					"	6 "
15. Indigestion or vomiting	"	"			"	4 "
Clinical Secondary deposits					"	12 "

Cough was present in the majority and this, as would be expected, is the observation of all

clinicians; it was prominent in fifty of the cases at one stage or other, and was the initial complaint in forty patients. When early it is as a rule due to the associated Bronchitis, and in the later stages to secondary infections giving Bronchiectasis or Pneumonias. When due to invasion of the mediastinum or to pressure on the recurrent Laryngeal nerve, it is "Brassy" in character and often paroxysmal, and may have associated with it marked swelling of the veins of the Head and Neck and transitory oedema. On occasions it is accompanied by intense dyspnoea resembling a bad asthmatic attack. At a later stage when the laryngeal nerve is paralysed the cough becomes husky and very weak. Severe paroxysmal cough of a very distressing character takes place when the trachea or a large bronchus is subjected to pressure with or without actual invasion; this type of cough Schröder⁹⁷ likened to that of Whooping Cough.

The cases in which cough was absent or insignificant were those with a very acute onset without bronchial or pneumonic signs.

Dyspnoea was present as an initial symptom in only six cases, and in all these Pleurisy usually with a rapidly accumulating effusion was found. In one case it was associated with a spontaneous Pneumothorax. Later various degrees of dyspnoea are nearly always present, possibly due to occlusion of a large

bronchus and the associated collapse of the lung or to Bronchiectasis, Broncho-Pneumonia, or some of the other complications. Reference has been made to the paroxysmal attacks of dyspnoea.

In some cases where extensive areas of the lung were affected and out of action, dyspnoea was not a marked feature during life, except perhaps as a terminal event, and it is difficult to know whether dyspnoea is actually ever due to an area of lung destruction or inactivity, provided the rest of the lung is efficient in its respiratory function. Inspiratory Stridor was present in a few cases, due to pressure on the trachea by infiltration or surrounding growth.

Sputum may vary from mucoid and clear, mucopurulent, purulent to blood streaked or frank haemoptysis. When Bronchiectasis is a complication it is large in amount and occasionally foetid. In rare cases carcinomatous cells may be found, and cases are on record where portions of the growth have been coughed up. Matthes⁷¹ considers the presence of fat globules in the sputum as a sign in favour of neoplasm but it has been found in Tuberculosis, Bronchiectasis and Diphtheria.

Haemoptysis was more common in my cases than in the majority of reports, being present in some degree and at one stage or other in just over

64 per cent. Maxwell and Nicholson found it in 55 per cent, and Davidson in 35 per cent.

In two cases it occurred as a brisk hemorrhage of acute onset, death supervening in one a fortnight later, and the other died of another severe haemoptysis five weeks later. In the chronic cases it was the immediate cause of death in three. Blood streaking of the sputum or small hemorrhages are possibly due to ulceration of the bronchial mucosa, while a large and brisk haemoptysis is due to erosion of a larger vessel in the growth itself or in a bronchiectatic or abscess cavity.

Pyrexia is usually found at some stage of this disease, and may be remittent or intermittent in type, less often it is continuous. In the majority there is a small evening rise resembling Phthisis, but rarely it is hectic and swinging and in these night sweats are common. As a rule the rise in temperature is due to purulent Bronchitis, Bronchiectasis or Pneumonia, but in quite a number of cases showing these complications on post-mortem there was no pyrexia during life, and inflammatory complications even with pus formation, as Empyema or abscess, may give no rise of temperature, showing that pyrexia by itself is of no significance in any case. As a rule, though not invariably, a Leucocytosis accompanies the pyrexia. Tachycardia, unassociated with pyrexia, was found in

some cases; this is probably toxaemic in nature, but may also be due to actual invasion of the myocardium, while vagal involvement has also been suggested as the cause.

Wasting history of a loss of weight was given in thirty five cases, but it was surprising how well nourished and bright many of the cases were in spite of marked physical signs, and extensive involvement of the lung as shown radiologically. In the rapidly fatal cases there was never wasting to any noticeable extent, but in the late stages of the chronic cases Cachexia was severe and had associated with it the usual anorexia, malaise and anaemia.

Pain was the first and prominent symptom in five cases, in three it was associated with Pleurisy, in one with Empyema, and in the other it was in the nature of an Anginal attack. It was also present in 55 per cent of the cases with a gradual onset. It varied in character from slight to severe and agonising, being described as "gnawing, stabbing and constricting, or a feeling of suffocation within the Chest." In distribution it was localised to small areas; to one side of the Chest, the whole Chest, or "like a band round the Chest." In others it was referred to the neck, shoulder and arms, back or abdomen. The cause of the lesser and chronic forms of pain is involvement of the pleura by the main

growth or metastases, and the strain of coughing; the more severe forms are due to acute pleurisy overlying the growth or to infarction of an area of the lung. The most severe type is due to erosion of the bony chest wall with invasion of the intercostal nerves, or from secondary deposits in the Spinal Canal pressing on the posterior nerve roots or the cord itself giving the characteristic girdle or stabbing pains. Pain may also be due to Pericardial involvement, secondary deposits causing irritation of some nerve plexus, or the thrombosis of larger vessels. In this series the Chest wall and intercostal nerves were affected in only one case, and the Brachial plexes also in one.

Dilated veins were seen over the Thorax, and to some extent over the Abdomen. Also in the Head and Neck, especially on coughing. This is due to Metastasis or infiltration of the Mediastinum causing obstruction of the Superior Vena Cava. Deist²³ states that this is an early sign, but as it is due to infiltration, it can hardly be otherwise than late.

Night Sweats are usually only found in association with the hectic type of temperature, and are of no special significance.

Cyanosis was rarely an early sign except in a slight degree, but as a late sign it was present in over 18 per cent, when its intensity varies according to the amount of pressure on, and congestion of the veins. According to Maxwell it is a sign of gross

pressure on the trachea, causing insufficient air entry with deficient oxygenation of the blood. In the last stages it may be intensified by the terminal complications.

Oedema is usually associated with dilated veins, and less often with cyanosis. It was most common in the neck and arms, showing mediastinal invasion or infiltration or thrombosis of the veins. The oedema may be unilateral and transitory. Local oedema of the Chest Wall occurs as a result of direct infiltration of the parietal pleura.

Dysphagia is practically always a late manifestation though in one case it was among the early complaints. It is due to pressure on the oesophagus by mediastinal Metastasis, or may be a sign of actual infiltration.

Laryngeal Paralysis. Voice changes varied from slight hoarseness to complete Aphonia, but in only one case was it found initially. The left Recurrent Laryngeal nerve was affected very much more often than the right, and this is due to its anatomical position. It runs through a group of glands situated between the Arch of the Aorta and the left Vena Anonyma, and it is when these glands are infiltrated that the Recurrent nerve is pressed upon. The corresponding group of glands on the right lies at

the bifurcation of the Superior Vena Cava into the two Venae Anonymae, and is in close proximity to the Phrenic nerve, accounting for earlier and more frequent right diaphragmatic paralysis.

Indigestion or Vomiting was an early complaint in one case. It may be due to Abdominal metastases, but more often is caused by the excessive paroxysms of cough. It has also been recorded with cerebral deposits.

Finger Clubbing of a minor degree occurred in a small number of cases. It may be a sign of diagnostic value in the absence of secondary lung infections and with no other condition found to account for it. Cases of marked Osteo-Arthropathy are frequently described in the literature, and Brunn¹⁶ emphasises the importance of a careful examination of the Pituitary gland in all such cases, as metastasis and a general hyperplasia of the Anterior lobe of this gland have been found.

Other Pressure Signs as inequality of pupils and exophthalmos indicative of involvement of the Sympathetic nervous system are reported. In one of my cases there was inequality of the radial pulse beats due to pressure on the Aorta, and this along with other factors led to an erroneous X-ray diagnosis of Aneurysm (see Case 10). Signs of Congestion of the

Brain, as severe headache, vertigo or convulsions, through pressure on the Superior Vena Cava were not noticed.

The paroxysmal Cough, Dyspnoea, Vomiting, and the upset in the Respiration rate in some cases apart from dyspnoea, have all been ascribed to irritation of, or pressure on the Vagus nerve, though the explanation is perhaps more obvious on the grounds mentioned in their discussion. Maxwell and Nicholson mention that in cases where the respiration rate is affected in this manner it is a point of diagnostic importance.

Metastases were discovered on clinical examination during life in twelve cases, mostly in the Supra-Clavicular, Axillary and Cervical glands, in the order mentioned, in the Liver in two cases, and in the Abdomen and Brain each once.

Duration of Symptoms.

It is obviously impossible to give absolutely accurate figures as to the duration, as the date of origin of the disease is never known. I have, however, calculated the duration as from the time of the first definite symptom up to the day of death, ignoring the presence of minor or indefinite symptoms of lengthy duration previous to this.

Duration of life after onset of first definite symptoms :-

Over 3	years	2 cases
" 2	"	5 "
" 1 $\frac{1}{2}$	"	4 "
" 1	"	11 "
" 6 months		21 "
" 3	"	12 "
Under 3	"	4 "

The average duration was 12.1 months.

The average duration after admission to hospital was 46 days.

The longest duration was 45 months, the shortest 3 weeks.

Walshe in 1871 in a series of 58 cases found the average duration of life 13.2 months. ⁷⁰ McBean Ross in an investigation of 60 cases at the Brompton Hospital found it 7 months. Maxwell and Nicholson ⁷⁵ gave their average as 10.9 months, and came to the conclusion that the direction and extent of infiltration had no influence on the prognosis as to the length of life. Though figures compiled on these lines show appreciable variations, the average shows that the expectation of life after diagnosis seldom exceeds one year. My experience agrees with that of Simpson that the longest durations are among the more elderly patients.

Physical Signs.

These will depend on the site of origin, the mode of spread, the stage of the disease when first examined, and lastly on the presence or absence of

complications. In the characteristic early case, say commencing at the hilum of the right lung, there may be no physical signs at first, or there may be a slightly impaired percussion note to the right of the Sternum for an inch or more between the 2nd and 3rd and 3rd & 4th intercostal spaces, over this area air entry may be weaker than in the corresponding area on the opposite side or the breathing may be bronchial in type with increased vocal resonance. Again in an early case where the Carcinoma takes origin within a bronchus, there may also be no physical signs, when the patient is examined for the first time for some complaint like slight haemoptysis. It is well known that the pathological processes determining Physical signs may give rise to vague or to definite symptoms long before reaching the stage of showing evident signs on examination; and so in cases of this description accessory methods of examination may prove the presence or absence of neoplasm, and the nature of such neoplasm if present. In some cases a mediastinal metastasis may be so extensive when first seen as to mask all signs in the lung and give the impression of being a primary mediastinal neoplasm. Quite a common finding is massive dullness on percussion usually confined to one side, with weak and distant or absent breath sounds. These signs are due to collapse of the lung following Stenosis of a Main Bronchus; if in such a dull area there is a patch where distinct

bronchial breathing is heard with accompaniments it suggests a Pneumonic area or possibly an Abscess. Physical signs of cavitation, unless showing evidence of rapid increase in size, are as a rule not found in Bronchial Carcinoma. To this, however, there are exceptions. It may occur after the presence of the disease has been established for some time, as in an abscess forming in necrotic carcinomatous lung tissue and communicating with a bronchus, or similar cavitation in secondary bronchiectatic conditions. Huguenin and Roux Lacroix⁴⁸ published a case in which a large solitary Cavity was present in the right upper lobe, the only symptom was haemoptysis, but a pathological fracture and the presence of tumour cells in the sputum showed the nature of the disease, though the authors were uncertain as to the origin of the cavity. Other workers, including Ewing, have reported Carcinoma arising in Tubercular cavities, though this must be a rare occurrence.

Pleurisy with effusion, though as a rule a late manifestation, may by its very definite physical signs mask the true nature of the disease, but certain methods of examination may overcome this difficulty.

Inspection.

In some early cases diminished respiratory movement may be noticed on one side of the chest wall. As a rule there is little or no abnormality in the

shape of the chest, though local wasting may be noticed. In late cases a fullness of one side may be seen when the growth is massive or when a considerable pleural effusion is present.

Palpation may show increase or absence of vocal fremitus; displacement of the Heart may indicate lung collapse, a large pleural effusion or a massive growth.

Auscultation perhaps gives the best information on physical examination. Diminished air entry on one side is often a very early sign due to some obstruction in a bronchus, or according to Maxwell due to bronchial spasm even before there is narrowing or obstruction. In other cases pleural friction may be found early. Adventitious sounds may occur with the various complications, of which the earliest is Bronchitis. Bilateral physical signs are suggestive of active pulmonary Tuberculosis or other chronic inflammatory condition.

From a consideration of the physical signs the following conclusions may be deducted. No physical signs are pathognomonic of Bronchial Carcinoma, but signs of diminished movement, diminished air entry, and other unilateral signs in an adult, in whom there is no other condition present to account for them, should rouse a very strong suspicion of the presence

of malignant disease of the lung, and all possible methods of examination should be resorted to in order to prove its presence or otherwise.

ACCESSORY METHODS OF INVESTIGATION.

Sputum.

The appearance and the frequency of the presence of blood have been commented on. In practically all cases Tubercle bacilli were examined for and in four cases were found present. In only two cases did the pathological report mention the presence of "clumps of oval cells" (see Case 4) suggestive of Carcinoma. In no case was the so-called "Currant jelly" type of sputum seen.

Betschaert¹¹ reported a few cases where a positive diagnosis of Pulmonary Carcinoma was made from fragments of tissue in the sputum, and he remarked on the rarity of it.

Pleural Effusion.

Pleural effusion was found in fourteen cases during life; in half the number it was clear, and in the rest it was blood stained; in two cases pus was found. The presence of blood in the effusion is not pathognomonic, but is very suggestive. The same can be said of the rapid re-accumulation of the fluid after removal. Bacteriologically it should be examined for Tubercle bacilli and if necessary intraperitoneally injected into a guinea-pig; the presence of

other infective organisms should also be looked for. Cytologically the fluid is also of interest though seldom of diagnostic importance. In some of the clear fluids red blood corpuscles were nevertheless present. The predominating cells were lymphocytes, though in a few polymorphonuclears were in excess; in one case the report stated "A great number of pleural endothelial cells, many bi-nucleate and a few multi-nucleate; polymorphs and lymphocytes in equal numbers - the picture suggests pleural Endothelioma." (see Case 6).

The presence of typical Foulis cells is held to be good evidence of malignant disease involving the pleura.

Seecof⁹⁹ claims to have made a diagnosis in agreement with subsequent autopsy in 79 per cent of a series of 38 pleural fluids taken from patients suffering from Bronchial Carcinoma. Fry²¹ has made some interesting observations on the flocculation reaction of the sera of cases of malignant disease with a saline emulsion of acetone insoluble, alcohol insoluble extracts of tumour tissue. Davidson reports that this test was tried on the pleural effusions of two of his cases with positive results. As Tuberculosis, Syphilis and Suppurative conditions have to be excluded, and the results are as yet very limited, judgment on its value cannot be passed. Taking everything into consideration the pleural effusion in this disease does not yield any distinguishing evidence.

Blood.

The count shows a minor degree of Secondary Anaemia in many of the cases. Polymorpholeucocytosis was found in the majority of cases in which some infective complication with pyrexia was present, though curiously it was also seen in other cases where no complications or pyrexia were present. This lessens its value as a differentiating point between Bronchial Carcinoma and lung Abscess, though it may be of some value in excluding Aneurysm unassociated with lung complications. The Wasserman reaction of the blood should be done in every case as a routine, for though a positive result does not exclude Cancer of the lung it must be remembered that Gumma formation or Syphilitic fibrosis in the lung may simulate it. It is of some value too in a case where Aneurysm is suspected.

Microscopical examination of material removed, either excised glands or by Bronchoscope, Thoracoscope or otherwise should in all cases be done for diagnostic purposes.

Lung puncture with a wide bore needle and microscopic examination of any material thus removed has been recommended, and Hellendahl⁴⁴ and others reported cases in which a diagnosis was made from material so obtained, but this method is hardly to be recommended as it may stimulate growth in the neoplasm, and direct infection may follow in the tract

of the needle; the more modern accessory methods of examination without these risks to the patient are preferable in every way.

Bronchoscopy in all cases with vague symptoms, especially appearing for the first time in adults at the age of 40 and over, with nothing definite to account for it, and referable to the Chest, this examination is a necessity. With combined Avertin and local anaesthetic there is very little or no discomfort to the patient. It is the only method by which early tumours in a bronchus, either malignant or benign, can be seen, diagnosed, and moreover, successfully removed in some cases. At the Royal Chest Hospital, London, I saw Mr Zamora remove an endobronchial growth by this method in a case of Dr Day. The patient had a history of occasional haemoptysis with a slight cough, there was very little sputum and Tuberculosis was excluded; on section the growth was described as a Fibro-papilloma.

In ten of my cases over the period 1930-1931 the diagnosis of Bronchial Carcinoma was verified by microscopical examination of material removed bronchoscopically, though they were all advanced cases in which there was no doubt of the diagnosis (see Case 9). Chevalier Jackson⁵² and his associates have described numerous cases in which an early diagnosis was arrived at by this method of examination. Manges⁷² lays stress

on the fact that the inhalation of non-opaque foreign bodies, in cases with no history, may give symptoms resembling Bronchial Carcinoma, and examination by this method may decide the diagnosis. Aneurysm must be definitely excluded before this examination is undertaken.

Thoracoscopy is done after the induction of artificial Pneumothorax, and in cases where a serous or hemorrhagic effusion is present replacement of the fluid by air or oxygen. It cannot be done in the presence of extensive pleural adhesions, and has only a limited application. It is a useful aid towards definite diagnosis in those cases where the growth is superficial in the lung, and in others may differentiate between growths of the lung itself, and growths of the pleura or Chest wall.

Exploratory Thoracotomy preceeded by artificial Pneumothorax, and carried out by an experienced surgeon is a matter of no more serious import these days than an Abdominal exploration, and as a rule the patient has less post-operative discomfort. As the interpretation of symptoms and physical signs in the Chest is a matter of comparative difficulty this operation should be undertaken more frequently, after close co-operation between physician and surgeon, if progress is to be made in the early diagnosis and treatment of intrathoracic tumours. Numerous cases

are on record, where suspected malignant disease after exploration has proved to be Teratomata or some other benign tumour or cyst, and these were successfully removed. In the absence of this method such cases would have been doomed by the gradual enlargement of the growth with consequent pressure symptoms, secondary infection of the cyst, or by malignant disease arising in the benign growth.

X-Ray Examination and Appearances.

Primary Bronchial Carcinoma, so often insidious in onset, may be present for a comparatively long period before its presence is suspected, and it is thus of extreme importance that all cases, even with the slightest of symptoms referable to the Chest, should be radiologically examined as a routine, as many Lung Cancers have in this manner been accidentally discovered, even in the absence of clinical manifestations. Atypical sign in any of the common Lung diseases should always suggest the possibility of malignant disease, and X-ray examination then constitutes one of the most important accessory investigation methods.

The examination should consist of observation of the patient under the screen at regular intervals to judge the range of diaphragmatic movement, and the manner in which the lung shadows vary during inspiration and expiration. The radiographs should be taken

in the erect position both antero-posteriorly and laterally, and the film taken by an apparatus sufficiently powerful to allow of a distance of 2 metres, and a maximum exposure of $\frac{1}{5}$ th of a second. As the appearances vary with the situation of the neoplasm, they are best described according to their anatomical position in the lung, and not as to their pathological characteristics, though this was attempted by earlier observers, as MacMahon and Carman.⁷⁶ The appearances are not by any means gross nor so markedly characteristic that their interpretation does not often call for the greatest care. Close co-operation between physician and radiologist is imperative, and the induction of artificial Pneumothorax and the injection of Lipiodol into the affected bronchus may on occasions be necessary before a definite conclusion can be arrived at.

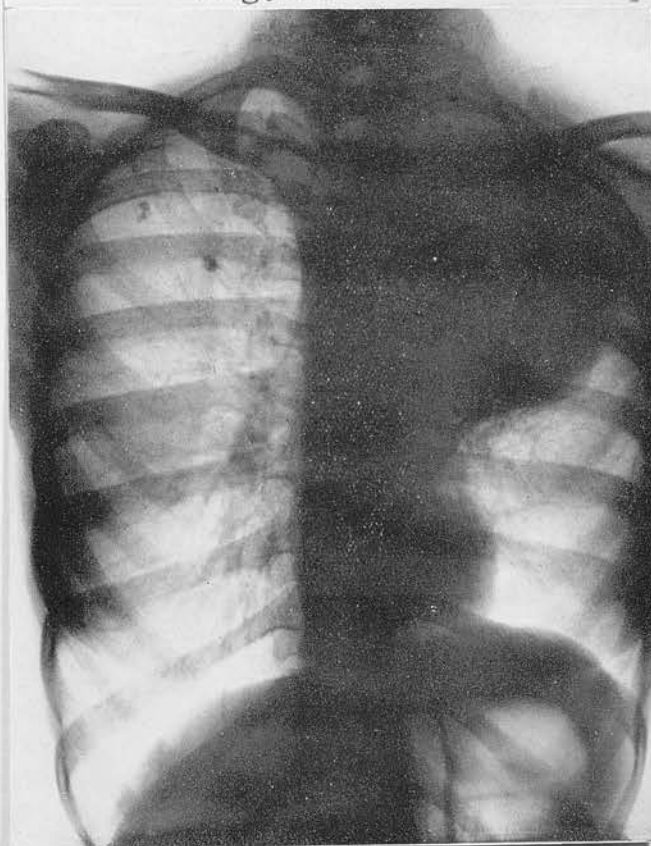
Melville⁸¹ gave a very serviceable classification into three main varieties.

1. Upper Lobe Carcinoma, in which this area of lung was collapsed due to obstruction by the growth of its bronchus, the shadow being sharply defined by the interlobar septum.
2. Hilar Carcinoma, where the neoplasm appears at the root of the lung and radiated from the central opacity in heavy linear striations, likened to a "rising sun." There is no collapse.
3. Lower Lobe Carcinoma in which the basal lobe is irregularly opaque, the pleura being usually early involved and effusion is a common finding.

Kerley⁵⁵ also gives a very simple classification, not differing essentially from that of other writers, but perhaps most adaptable to the usual findings. His three divisions are Lobar, Hilar and the rarer Nodular varieties. More recently he has advocated, for reasons of greater simplicity, to have only two divisions, in either of which form this disease was most commonly seen, namely the Lobar or Pneumonic, and the Hilar. "The former being due to a "combination of growth plus collapse and the latter "to growth minus collapse." This latter is often converted at a later stage of the disease into the first named. In the Lobar type a lobe or the whole lung becomes atelectic as a result of Stenosis of a main bronchus, and malignant invasion of the collapsed lung follows in time. When the right or left upper main bronchus is the seat of disease and becomes partially occluded, the lung becomes collapsed at the apex or at the periphery just below the clavicle, but this comparatively early stage is not often seen. When the occlusion is complete the whole lobe becomes homogeneously opaque, the interlobar fissure forming the lower border of this opacity (Figs. A & B). The resulting contraction of the lobe as seen by the upward displacement of the fissure shows that the thoracic contents are diminished, and the Heart and Mediastinum move to the affected side. This displacement of the Heart and Mediastinum is, unlike that due to

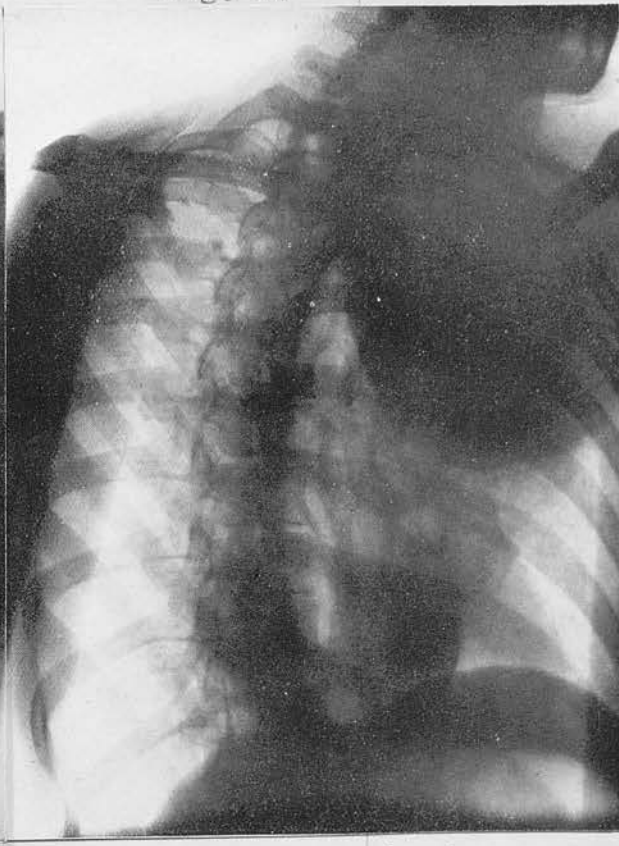
fibrosis, exaggerated on deep inspiration. When the growth affects the right upper lobe the corresponding phrenic nerve is often involved, while if the left lobe is the seat the left Recurrent Laryngeal nerve is affected. The reason for this has been discussed. When the phrenic nerve is paralysed the affected side of the diaphragm takes a higher position, and shows diminished paradoxical movement before the final stage of cadaveric immobility is reached. When this or Recurrent paralysis is found with a collapsed lobe, it is very suggestive of Bronchial Carcinoma. Abscess formation is not so common in upper lobe Cancers nor are pleural effusions. Enlarged Mediastinal Glands can often be demonstrated.

Fig. A.



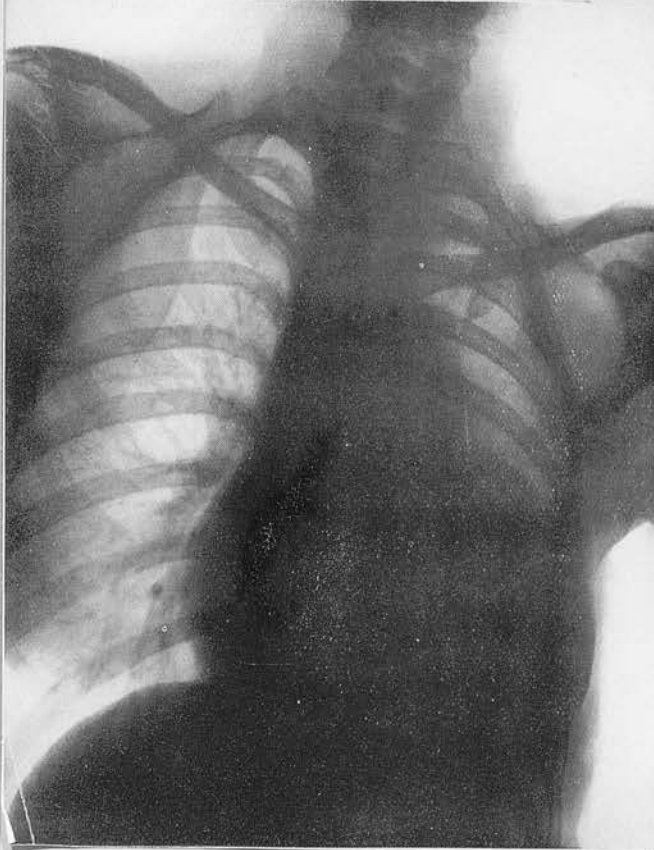
"Lobar type" of left upper lobe.

Fig. B.



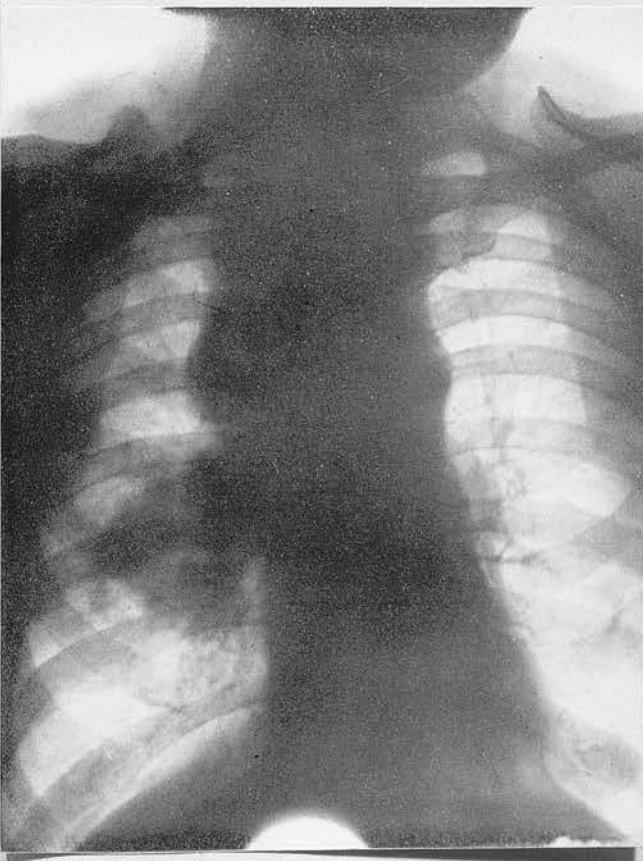
Lateral view of same Case showing strict lobar delimitation.

Fig. C.



Carcinoma left main Bronchus.
Lower lobe collapsed. (Lobar type.)

Fig. E



Carcinoma right main Bronchus eroding
the bronchus & invading the alveolar tissue.
Enlarged glands immediately above growth.

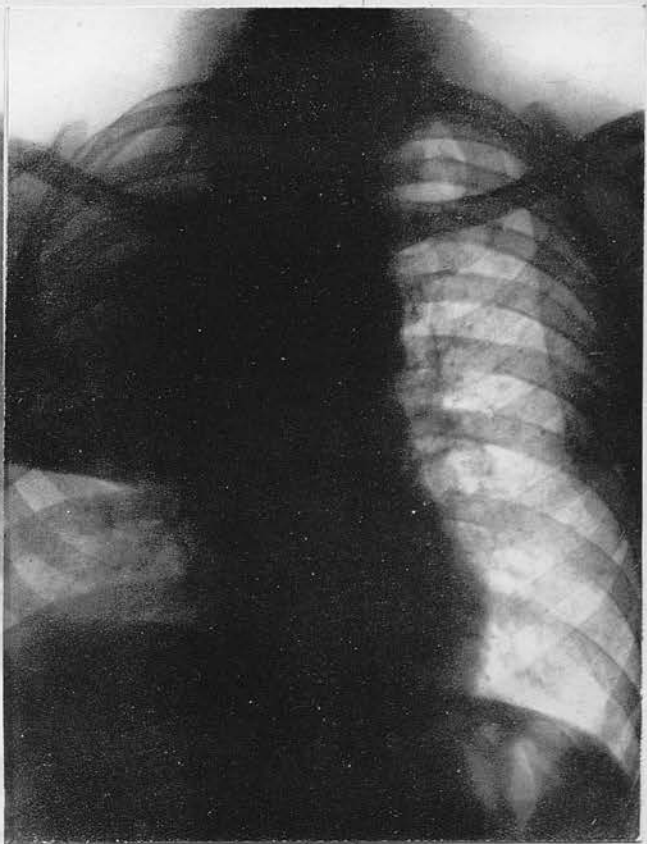
Fig. D.

80a



Same case after short interval - whole
lung collapsed. The shadow at the right
base is lipiodol. (Lobar type.)

Fig. F.



Carcinoma right upper lobe with
paralysis of Diaphragm. (Lobar type.)

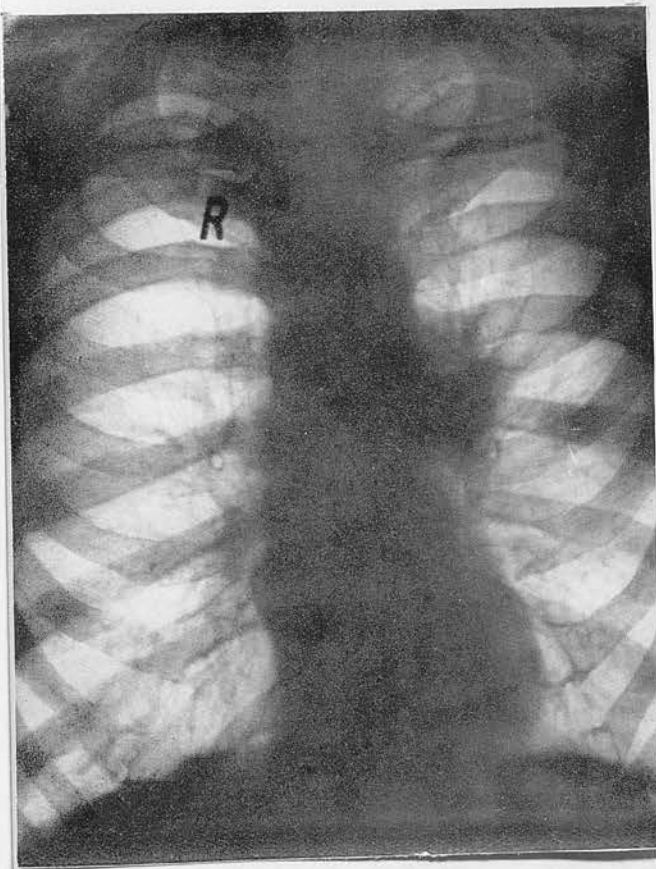
In the lower Lobe, Carcinoma also causes a similar opacity, bounded above by the great fissure and below by the diaphragm, - a lateral view showing the demarcation better. The mediastinal deviation during respiration is as a rule better marked than in the upper lobe; the diaphragmatic movements, however, are more difficult to detect, especially so when a large associated pleural effusion is present. On the left side this may be overcome to some extent by the administration of a Seidlitz Powder to the patient to cause gaseous distention of the stomach. When the whole lung is collapsed a complete opacity very like that shown by an extensive pleural effusion is seen (see Fig.D). Unlike pleural effusion, however, the Heart and Mediastinum are displaced towards the affected side, the intercostal spaces are narrow and the mediastinum moves towards the affected side on inspiration. Pleurisy with effusion is a very common complication, and though the fluid may prevent the characteristic mediastinal movement during inspiration, it never displaces the Heart and Mediastinum to the opposite side as in simple pleural effusion. Bronchiectasis of various degrees usually occurs in the collapsed lung, but the occlusion of the bronchus usually prevents its detection during life. Abscess may develop and if air be present a fluid level in a circular opacity may be seen, but this, owing to

Stenosis and resulting collapse, is rare. A distinguishing feature in the diagnosis of abscess, apart from obvious malignancy, is that simple lung abscess is symmetrically surrounded by an area of congested lung tissue. The formation of a large cavity due to tissue breakdown in the major part or the whole of the collapsed lung area will, in the absence of a history or of metastases, be impossible to distinguish from an ordinary abscess. The presence of mediastinal or large bronchial glands is a valuable diagnostic point, mediastinal metastases on the right side must be looked for on that side of the hilum and just above the ascending Aorta, on the left side in the hilum between the arch of the Aorta and the Pulmonary artery. Invasion of the paratracheal glands widens the shadow of the upper anterior Mediastinum. In cases where dysphagia is a complaint, a Barium meal film may show infiltration of the posterior Mediastinum or the oesophagus itself.

Hilar type is characterised by a homogeneous, dense, semicircular opacity in the hilar region, the outline is as a rule irregular with wavy striations into the normal lung tissue. Sometimes it has a more sharply defined border, in either case the absence of inflammatory reaction in adjacent lung tissue is noticeable. This type is due to growth arising at or near the bifurcation of the trachea; it does not occlude

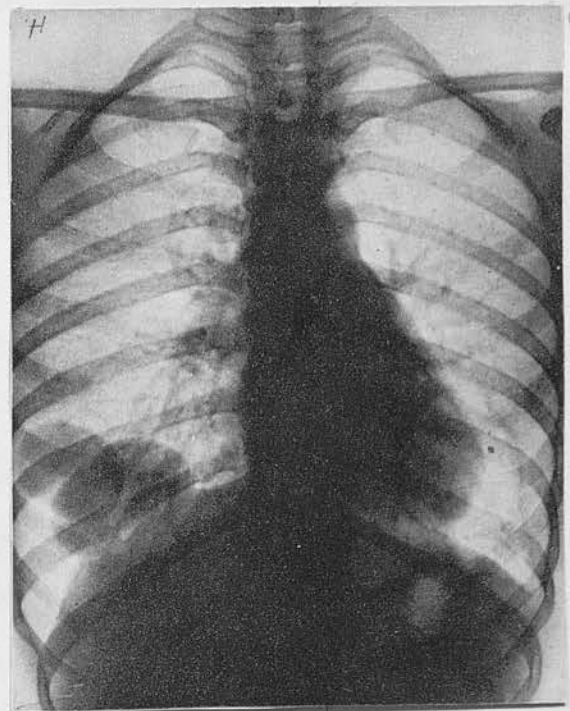
the bronchus, but gradually erodes it, invading all the surrounding tissue and glands, explaining the massive appearance seen on a film. When the outline is sharp it may closely resemble the shadow given by a Dermoid or Hydatid Cyst, though the latter is usually situated in a lower lobe; the Clinical findings Metastases or the result of complement fixation tests are important diagnostic points in such cases. Pulmonary Syphilis may manifest itself as a hilar opacity but there is always gross emphysema in the surrounding lung tissue.

Fig. G.



Early Carcinoma of Hilar variety of left lung.

Fig. H.



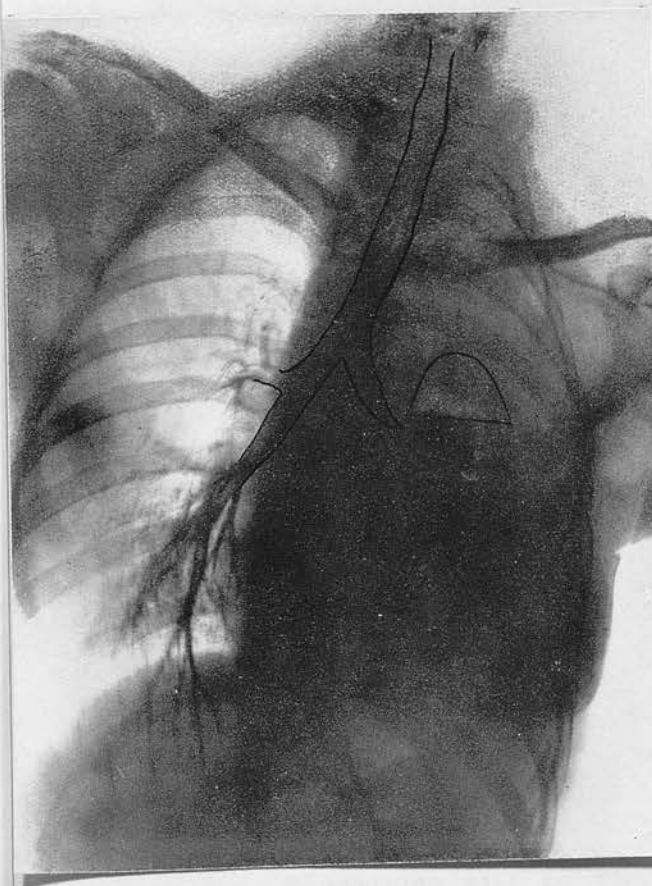
Typical appearance of Hydatid cysts at base of right lung.

In some cases of Aortic Aneurysm it may be difficult to differentiate clinically or radiologically from either the Lobar or Hilar type of Bronchial Carcinoma. The Aneurysm may cause a rounded shadow almost lobar in distribution on the left, and in some cases on the right side of the Chest, the surrounding zone of lung being of normal density, or it may compress a bronchus giving a lobar collapse. It may also be seen as a Hilar shadow with a semicircular, well defined edge. Many such cases are described, and a very good illustration of one is given by Clerc, Deschamps and Schwob,¹⁹ where a dissecting aortic aneurysm found post-mortem was diagnosed clinically and radiologically during life as Pulmonary neoplasm. In one of my cases (Number 10) an erroneous diagnosis of Aneurysm was made on the radiological appearances. The coexistence of the two conditions has been mentioned.

The Nodular type appears as an irregular, ragged opacity situated in one lobe, or multiple and scattered throughout all the lobes. They are usually circular, seldom sharply defined, and from one to three inches in diameter. Coarse striations may run from these opacities towards the hilum, which is invariably thickened by enlarged glands. The appearance is somewhat like that caused by Actinomycosis, but in the latter condition the opacities are denser and the radiating striations run in all directions, and not towards the hilum alone, while the hilum is

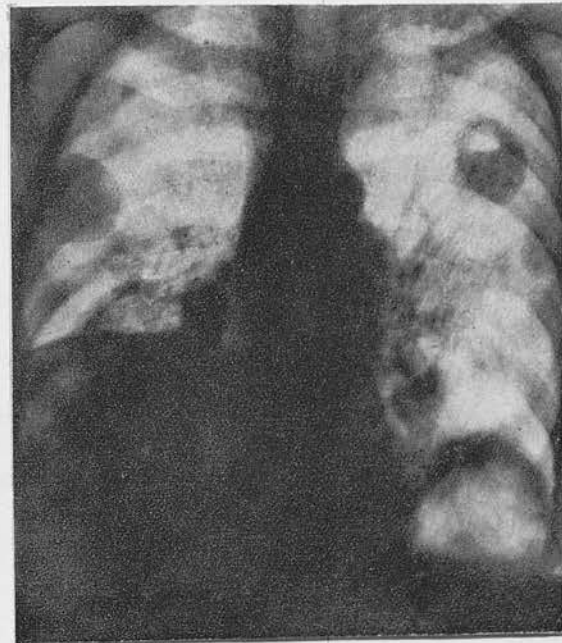
never much enlarged. They resemble secondary nodules in appearance, and it has often been shown that they are secondary to a small, hilar carcinoma. I have never seen this nodular form as a primary growth radiologically, and have always taken their presence in a film to indicate metastatic growths, which when early were small, circular, slight opacities, becoming sharper and more opaque the longer their existence. ⁵⁵Kerley appears rightly to have dropped this radiological type as a primary carcinomatous manifestation.

Fig. I.



Lipiodol showing stenosed Bronchus. There is abscess formation as shown by the fluid level.

Fig. J.



Secondary Neoplasm of lung - one shows degeneration with a fluid level.

Lipiodol.

X-ray examination following the intratracheal injection of Lipiodol is often of great diagnostic value. In earlier cases it may show irregularity of the bronchial lumen due to the growth; in late cases it shows partial or complete occlusion of the bronchus, the iodised oil failing to enter the bronchi below the obstruction. In lower lobe cases it shows the point of stenosis in a striking manner, and in cases where the underlying condition is masked by pleural effusion, it shows clearly through the opacity caused by the fluid. In upper lobe lesions, it is not applicable even with inversion of the patient, as the density of the oil causes it to run out when the patient is placed in the correct position for taking a film.

Artificial Pneumothorax is advisable for radiological diagnosis, where an excessive pleural effusion obscures the underlying condition in the lung. In the presence of extensive adhesions complicating the neoplasm, complete collapse is impossible, and this very fact may be of assistance when taken in conjunction with other diagnostic features. Even partial collapse may give information as to the relation of a tumour, diagnosed by other means, to the neighbouring structures and to the lung itself. Its induction prior to Thoracoscopy and to Exploratory Thoracotomy has been mentioned.

DIAGNOSIS.

In discussing the diagnosis stress will be laid on such symptoms and signs as are considered to be early, and the presence of which, even in the absence of anything definitely diagnostic on physical examination, should arouse a suspicion in the mind of the clinician of the possibility of Bronchial Carcinoma. This suspicion should then stimulate further examination by all the ancillary methods described, and applicable to the particular case, the relative merits of these having been mentioned.

Early diagnosis may not only have been impossible, but may also have been considered unnecessary and useless in the days before the discovery of the various accessory examination methods, on account of the rarity this disease was then thought to be, and also because of the hopeless prognosis. The inaccessible nature of the site of origin, and the liability to infiltration of vital structures made successful surgical interference in those days appear well nigh impossible. Thoracic surgery has certainly advanced since then, and other methods of treatment found and improved upon, but the site and nature of Bronchial Carcinoma still make any but palliative treatment

impossible in the advanced cases. It is only in the early stages of the disease, before infiltration or metastases are established, that radical surgical measures are applicable, and it is thus a necessity that a reasonably accurate diagnosis should be made at an early stage of this intractable form of malignant disease, in order to make it amenable to surgery and to stimulate further interest in the efforts to find satisfactory methods of treatment.

In attempting to come to an early diagnosis the history is seldom of much value, though more than ordinary exposure to irritants and chronic lung affections should be noted. The early symptoms are cough, dyspnoea, haemoptysis and pain. When cough and haemoptysis, however slight, with or without other symptoms develop for the first time in a patient at or over the age of forty, Bronchial Carcinoma should always be excluded even if Pulmonary Tuberculosis or other pulmonary conditions causing similar symptoms be proved present. The "brassy" or husky cough of laryngeal irritation and paralysis may on rare occasions be an early manifestation of an otherwise latent Pulmonary Cancer, but it is a late stage in the disease, and a contra-indication for surgical interference. The same applies to dysphagia.

In some cases with an acute onset, the initial manifestations may be that of some pulmonary complication, as Pleural effusion, Pneumonia or Abscess; in

others it may be that of a metastasis as a lesion of the Central Nervous System or the Abdomen. All such cases belong to a group where early diagnosis, with a view to treatment, is impossible, though a correct diagnosis can usually be arrived at if the possibility of this disease is kept in mind, and the patient is in a condition to allow of the various methods of examination to be employed. Goldstein³⁶ says that "Bronchial Carcinoma should always be thought of in a case of an elderly patient with symptoms of abscess or gangrene of the lungs. If recent Pneumonia or inhalation of foreign bodies can be excluded, Carcinoma is probable, and if the onset of the illness was characterised by cough, loss of weight and a little slimy sputum occasionally blood stained, Carcinoma is certain."

The only physical sign of importance in early diagnosis is weak air entry over one lobe or lung, also unilateral signs developing for the first time in a patient near or over forty years of age should incite suspicion. An increase of the respiration rate well above the normal, and sustained after some days rest in bed, in a patient without obvious dyspnoea, is held by many to be suggestive of early Bronchial Carcinoma. Clubbing of the fingers, even in the absence of other more obvious symptoms or signs, is held by others to be an early sign - this is not my experience.

In differentiating the various conditions that may simulate Bronchial Carcinoma or obscure a correct diagnosis, it is found that the complicating conditions of the disease itself, are often the greatest source of difficulties; thus Pleural effusion and Pleurisy are frequently diagnosed. When the effusion is blood-stained and re-accumulates rapidly after removal it is presumptive evidence of neoplasm; the cytology of the fluid gives little or no evidence; metastases if present will be diagnostic, Thoracoscopy or Thoracotomy will show the cause of the effusion, and the radiological appearances with or without Lipiodol may make the diagnosis absolute.

Primary Lung Abscess can be excluded by the absence of a history of the inhalation of a foreign body, by absence of recent Pneumonia, and Bronchosopic examination to exclude the presence of a non-opaque foreign body; the presence of metastases is diagnostic and the X-ray examination may show its true character, though in some cases an absolute differentiation may be impossible during life.

Interlobar Empyema.

It is not always possible to locate this condition by physical examination or the exploratory needle, and in such cases where there is failure to find pus in the presence of pyrexia, leucocytosis and toxæmia, with signs suggestive of consolidation, a

suspicion of neoplasm arises. X-ray examination may decide the issue, but in rare cases Exploratory Thoracotomy may be the only method to make sure.

Chronic Bronchitis in a middle-aged patient without apparent or definite cause, or where the symptoms are at all atypical, should also suggest the possibility of primary Bronchial Carcinoma. Here the presence of haemoptysis will be indicative, and that of metastasis conclusive, of carcinoma. In the absence of metastases X-ray examination may give the necessary information, failing which examination by the Bronchoscope will be necessary.

Pulmonary Tuberculosis.

Attention has been drawn to the supposed etiological significance and to the frequency of reports regarding the co-existence of the two diseases. Lynham⁶⁹, and more recently Hurrell and Dawson-Walker⁵¹ have demonstrated the frequency of Pulmonary Carcinoma in Sanatoria post-mortems, unsuspected during life, in some cases associated with Tuberculosis, but in a few unassociated. The presence of Tubercle bacilli in the sputum or pleural effusion shows that there is active Tuberculosis, but does not exclude Bronchial Carcinoma. Conversely the absence of these bacilli cannot be held to exclude Tuberculosis absolutely, though if not found after frequent and repeated examination, in the

presence of haemoptysis, pain and dyspnoea, displacement of the Heart and Mediastinum towards the affected side, and unilateral physical signs, Bronchial Carcinoma is indicated. If in addition pressure symptoms or signs are shown, Tuberculosis may practically be excluded. The microscopical examination of glands, if present, may be diagnostic, and in the majority of cases the X-ray appearances of the two conditions are definitely dissimilar and decisive.

Haemoptysis as the only and primary symptom in an adult, in whom no obvious cause is apparent or definitely found on examination, should always suggest the possibility of pulmonary neoplasm, and the importance of Bronchoscopic examination in such cases cannot be overstressed from the view of both diagnosis and treatment.

Cerebro-Spinal Lesions.

The sudden onset of Hemiplegia or Paraplegia may represent the only and primary manifestation of this disease, Such cases when seen in a state of coma may be diagnosed as Cerebral Embolism or Thrombosis, and the true nature of the disease may be unsuspected and unknown, unless a post-mortem examination is made and the origin of the disease discovered. Many such cases are on record, and Ferguson and Rees³¹ recently published an interesting series.

Aneurysm may present considerable difficulty

in the differential diagnosis. Both conditions predominate in males, pain and pressure signs and symptoms are present in both; tracheal tug and expansive pulsation may be present or absent in either. Diastolic shock, Aortic thrill and murmur with a booming second sound, an age incidence of 35 to 40 years, and a positive Wassermann reaction are strongly suggestive of Aneurysm, though it does not exclude Carcinoma.

An age incidence over 40 years, haemoptysis, and dilated Thoracic veins in addition to other symptoms and signs, favour Bronchial Carcinoma, but do not exclude Aneurysm. Wasting, pyrexia, leucocytosis, sputum and hemorrhagic and rapidly accumulating pleural effusion favour Carcinoma. When an Aneurysm constricts and later actually occludes a large bronchus the diagnosis is still more in doubt. Though in most cases the X-ray picture of the two conditions are distinct, the difficulties of radiographic diagnosis may also be great; these have been discussed elsewhere. Bronchoscopic examination is contra-indicated unless Aneurysm is definitely excluded. The possibility of the two conditions co-existing must not be lost sight of. Simpson reported two such cases; he further states that the erroneous diagnosis of Aneurysm was made during life in five of his series of post-mortem cases of Bronchial Carcinoma.

Pulmonary Syphilis.

The possible co-existence has been referred to, as also the X-ray appearances and differentiation. A positive Wassermann reaction does not exclude Carcinoma, and when present the result of Anti-Luetic treatment may clear up the diagnosis.

Pulmonary Mycosis.

The presence of a Saprophytic organism in the sputum does not exclude Carcinoma, and usually it is a superadded infection; the X-ray examination is of importance and is referred to.

Benign Neoplasms; X-ray examination, after artificial Pneumothorax when in doubt, show that these tumours are invariably extra-pulmonary.

Cysts.

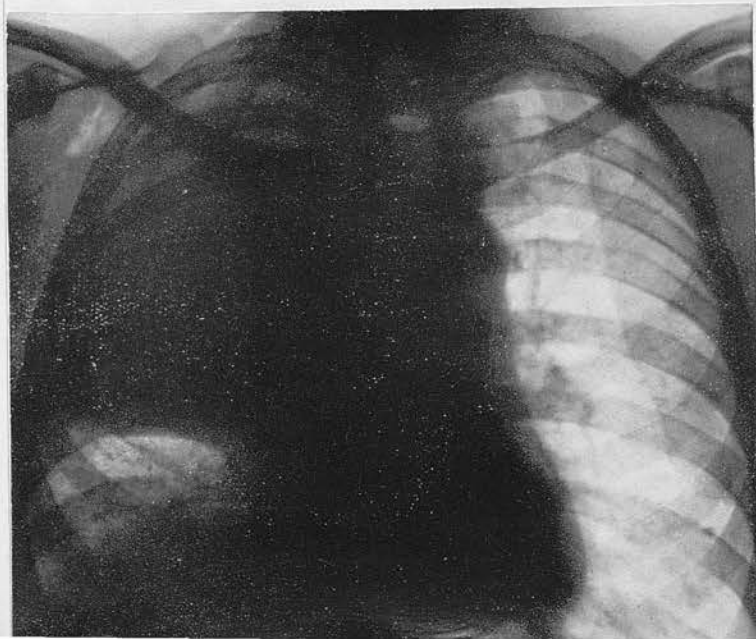
X-ray examination shows these as well-defined circular opacities; if anything they may be mistaken for secondary growths, but rarely for primary. In case of Hydatids an Eosinophilia, site in right lower lobe or mediastinum, positive complement fixation test (Bordet Gengou reaction) make the diagnosis certain. Aspiration of the Cyst is to be avoided.

Teratomata or Dermoid Cysts are more irregular in shape, Anterior in position and often adherent to the lung tissue. A lateral X-ray view invariably shows the growth to take origin in the Anterior Mediastinum. Induction of artificial Pneumothorax may show

up the relationship of the tumour if not clear. In rare cases Exploratory Thoracotomy may be necessary for definite diagnosis, and in doubtful cases it is always advisable for reasons already given.

In Lymphosarcoma and Lymphadenoma where the mediastinum is invaded a differential diagnosis may be impossible. If metastatic glands are found, excision and microscopical examination will settle the issue. In the absence of this in Lymphadenoma, enlargement of the Spleen, a Pel-Epstein type of pyrexia, and the blood picture may be decisive.

Secondary Malignant Growths in the absence of evidence of a primary source, and especially if confined to one lung, may give an exactly similar clinical picture. The X-ray appearance with the circular shape and sharply defined edges, and the usual multiplicity, are characteristic as a rule, though in rare cases, as the illustration below shows, it may be indistinguishable from primary Bronchial Carcinoma.



*Melanotic sarcoma
skewing right upper
Bronchus with
diaphragmatic par-
alysis. Six years
after removal of
eye for "malignant
pigmented tumour."*

TREATMENT.

Bronchial Carcinoma is perhaps the most distressing of all forms of malignant disease, both on account of its inaccessibility and its close relation to vital structures. The onset and course, on occasions so insidious, and the consequent late stage at which a positive diagnosis was made, together with the lack of the accessory examination methods, did not stimulate interest, nor was any adequate treatment employed except for the relief of symptoms. The difficulties then, of successful surgical removal or adequate irradiation, were obvious. It is only within the last ten years that definite attempts at surgical intervention have been made, and with enough success to warrant that this advance in thoracic surgery should act as a challenge to the medical attendant and clinical pathologist to diagnose Bronchial Carcinoma at a sufficiently early stage, in order that results may be so far improved upon as to make Lobectomy the treatment of choice. Naturally there will always be a large proportion of these cancers which may not be amenable to surgical treatment on account of their site of origin and situation, or because of the presence of early metastases or infiltration, and

recent improvements in the technique of Radium and X-ray therapy, and their application to these types of growth will be mentioned.

Surgery.

Thoracic surgeons agree that the type of carcinoma most amenable to Lobectomy is the Central or Parenchymatous, corresponding to the Nodular type of the radiological division. Unfortunately this type forms a very small proportion of the cases; Tudor Edwards²⁶ found only nine in his series of 118 patients. Six of these were inoperable on account of metastases, but the remaining three were successfully operated on by him. Certain ones of the Lobar type, especially of the lower lobes of the lungs, may under certain conditions also be classed as operable.

The majority of the Hilar type, involving as it does a main bronchus, offer little hope for successful removal on account of its close proximity to the mediastinal glands, and also because of the intense shock that would be associated with the removal of a large main bronchus and its corresponding portion of the lung. In growths of this type, taking origin in second or third degree branches of the bronchi, there is a better chance, and successful cases are on record. Tudor Edwards in his series describes the successful removal of a circumscribed neoplasm of

this variety, the patient being well and symptomless eight months after operation. Brunn¹⁶ found twenty-eight cases of successful surgical removal in the literature, and cites two cases of Sauerbruch, in which the patients were living five years and three years respectively after the operations. This was in 1926, and since that time many more successes have been added to this number. Surgical removal of early Endobronchial Cancers by means of the Bronchoscope, and the work in this connection by Chevalier Jackson and his associates, has been referred to.

Rist and Rolland give the opinion that future advances in the treatment of early diagnosed Bronchial Carcinoma will be made in the direction of Endobronchial surgery.

Radium Therapy.

On this subject I cannot write from any personal experience, but the consensus of expert opinion seems to be that this is the method of choice in cases where Surgery is impossible. The application of massive doses (1 to 4 gms.) in a bomb at a distance is the easiest method as it does away with any necessity for operation; but Tudor Edwards failed to see any improvement in six of his cases in whom this method was tried. The majority of radiologists seem to have discarded this method as unsuitable. External plaques may also be tried, but the depth of the growth

as a rule militates against its success; as a palliative, however, in those rarer cases in which the Chest wall is actually invaded, it has been found useful, especially in relieving the acute peripheral pain.

The insertion of Radon seeds was tried in two cases in my series; in one the seeds perforated the bronchial wall causing the patient a good deal of distress, and they were subsequently removed with great difficulty. In the other, where the growth was more central, the seeds were introduced more successfully, and there was amelioration of the symptoms during the four months after it that he lived.

Observers like Davidson and Edwards, who have had an opportunity of trying this method in a comparatively large number of inoperable cases, feel encouraged by their results, in relieving symptoms and prolonging life, to advocate perseverance with this method of treatment in selected cases.

X-Ray Therapy.

As to the value of this method of treatment there is at the present moment a great diversity of opinion, not only among physicians and surgeons, but among radiologists themselves. Nothing definite as to the results of this treatment can at this stage be arrived at, owing to the conflicting experiences of the experts; but it can safely be said, that in a

small proportion of cases of Bronchial Carcinoma there has been some improvement in symptoms and in the general condition of the patients, as a result of this treatment.

The more recent work in the use of Activated Fluorescin in conjunction with deep X-ray therapy gives promise of success in cases which had previously failed to respond to irradiation methods alone.

Copeman²⁰ has reported very good results in Breast Carcinomas in inoperable cases, and also claims a cure in three operable stage cases. At the Royal Northern Hospital in London, where patients from the Royal Chest Hospital attended for X-ray therapy, the technique for use in Lung cases as given by Goldesbrough³⁸ is as follows:- Sodium Fluorescin 5 per cent, Sodium Bicarbonate 3 per cent in normal saline. 20 c.c. of this is injected intravenously fairly slowly, taking three minutes, and exposure to X-rays takes place immediately after the injection. It is too early as yet to pass judgment on the results obtained by this method, it is sufficient to say that all cases so far treated have been inoperable ones in the last stages with marked symptoms and signs, and in at least half of the twelve cases of Bronchial Carcinoma I saw treated by this method there was improvement in the symptoms and general condition. The number of cases was too small, nor had I the opportunity of keeping

them under observation for a sufficiently long time to come to any conclusions as to the time this improvement lasted, and whether it actually prolonged life. Maxwell and Nicholson found in sixteen of their cases treated by irradiation alone that the average duration of life was fourteen months, compared with an average of 10.9 months for the whole series. F. Roberts⁹² claims "undoubted material benefit as regards alleviation of symptoms and prolongation of life." Davidson while stressing the limits and disappointments of this method is convinced of the "undoubted benefits of X-ray treatment in primary lung Carcinoma."

Chandler,¹⁷ who has had a very large experience of this type of tumour agrees with the extreme view of Tudor Edwards "that this method of treatment has proved very disappointing, and I have yet to see a patient who has benefited thereby," though he admits of its use to a limited extent in diminishing secondary deposits in the lung.

I only had occasion to see Lead Selenide injections used on two patients; in one there was an alarming reaction (see Case 2), and in the other none whatever. Most of the workers on Colloidal Lead, however, held that Bronchial Cancer was a contra-indication to this method of treatment.

I do not propose to enter into the details of Symptomatic treatment except in so far as to agree

with Chandler, cited by Davidson as to the value of Cocaine hydrochloride ($\frac{1}{4}$ gr.) as an adjuvant to Morphia, in the relief it gives in the very severe and urgent dyspnoea of the final stages.

There is, in my view, every indication that the abandonment of all hope with a diagnosis of Primary Bronchial Carcinoma will soon be a thing of the past, and with the definite efforts now being made at earlier diagnosis and more active treatment, a rosier prognosis will be possible in the near future.

CASE HISTORIES and POST-MORTEM REPORTS.

CASE No.1. A.F. male, age 44. Scalemaker's fitter.
Admitted to Royal Chest Hospital 18.X:28

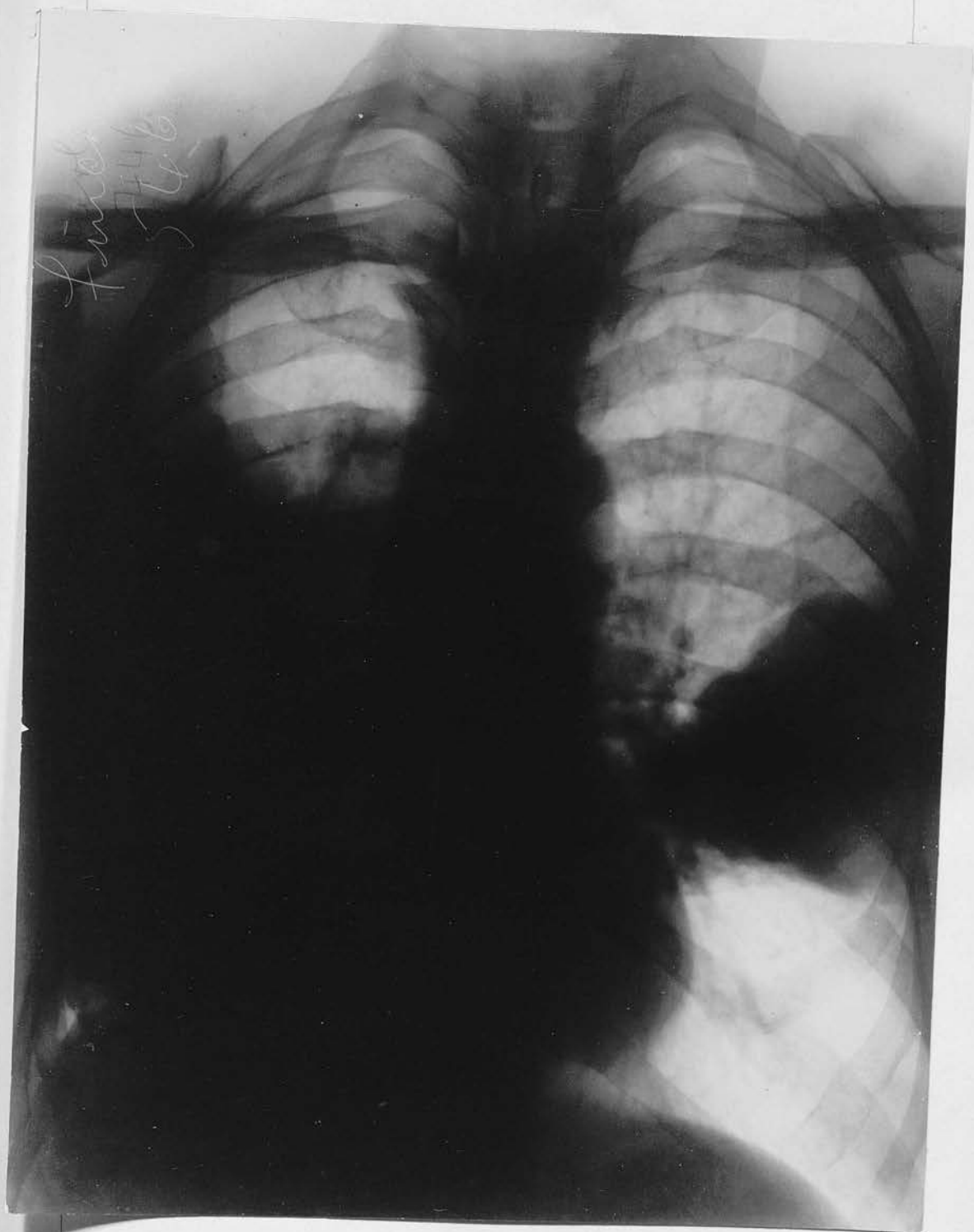
History. Cough for last two years with a frothy sputum; pain in left chest; dyspnoea on exertion getting worse - no marked loss of weight.

Exam. Extensive absolute dullness over lower third of right lung; breath sounds harsh, resonance of nasal tone. 10 c.c. straw-coloured pleuritic fluid removed for examination. Weight 9 st. 6 lbs. No enlarged glands.

Pathological Report Cell count large mononuclears 83%. Small lymphocytes 16%. Polymorphs 1%; a few Red blood cells, a few multinucleate cells. No tubercle or other organisms. Culture a gram negative Staphylococcus did not ferment any Sugars.

26.10.28 X-Ray. Heart normal position. Trachea displaced to right side. Diaphragm immobile on right, slow on left. Right Lung pleural effusion, Left Lung peculiar triangular consolidation of lower zone with irregular edges either metastases or encysted effusion ? (See Fig.I.)

Fig. I.



(28

(30:10:28. Right Chest aspirated, $\frac{1}{2}$ pint withdrawn
on each occasion.

Pathol. rep. injected into guinea-pig
with no evidence of Tuberculosis on
post-mortem.

3.11.28. Wassermann negative. Sputum negative for Tubercul. Bacilli on seven occasions.

While Blood Count 8800 Polymorphs 62%
 Small Lymphocytes 32%
 Large " 3%
 Large Mononuclears 2%
 Eosinophils 1%

22.11.28) 500 c.c. fluid aspirated and replaced with
 &) air.

3. 1.29) X-ray Report: fair collapse of right lung:
 middle and lower zones
 apparently consolidated:
 little change in left lung.

14.1.29. Blood Count R.B'es 5,790,000 W.B'c. 7000
 H.B. 98%

28.1.29. Weight 8 st. 8 lb.

He was discharged after this and received Deep X-ray Therapy at the Royal Northern Hospital. He was readmitted on 3.1.1930, having become suddenly "very short of breath, feeling like lump in his chest" "alternating with a feeling of tightness," no marked pain, appetite very poor, greyish colour, weak and drowsy.

On examination: T. 99.8° pulse 120 R. 30 dyspnoea at rest and has to sit up. Slight Cyanosis. No enlarged glands, right side of chest very flattened and diminished movement, and very poor air entry; at base breath sounds absent while at both apices anteriorly breath sounds were harsh. On left side dull area, with somewhat resonant note in centre - metallic tinkling sounds.

12.1.30. X-ray Report. Heart and trachea displaced to right side. Diaphragm fixed on right side, very slow on left.
 (See Fig.II)

Right lung Pleura thickened over whole lung.

Left " The opacity has increased in
 area, having a varying density
 but still fairly sharply defin-
 ed, suggesting Neoplasm or
 interlobar Empyema.

29.2.30. Patient died.

Fig. II.



Post-mortem Report.

Right pleura - thick, fibrous and adherent over whole surface. Right lung collapsed and fibrotic, irregular solid portion spreading from hilum into middle and lower lobes; translucent appearance and of pale grey mucoid consistency.

Left pleura - 10 2 clear fluid, recent adhesions with signs of acute inflammation on the surface. Left lung. In lower part of upper lobe is a wedge-shaped solid area of the same grey mucoid appearance. There is no bronchial obstruction in either lung, no bronchiectasis or Tuberculosis; no secondary deposits. Microscopical Examination.

A polygonal-celled Carcinoma with much irregularity in shape and size of cells. The consolidated areas have numerous Carcinoma cells within the alveoli, with mucin secretion present.

Case 2.

T.W. Male aged 58. Newsagent: admitted to Royal Chest Hospital on 20.5.1931.

Previous illnesses: Bronchitis often.
Pleurisy on left side. Pneumonia.

Family: Father died of Cancer of the throat.

Mother died of Cancer of the liver.

Present history. Cough for many years,

mostly at night, small quantities of sputum, no blood, pain for last six months across front of chest, dull in character and getting worse; very breathless on exertion; night sweats. Lost 2 st. in weight in last six months.

Examination.

Pale, wasted appearance with husky voice, fingers clubbed, glands in left axilla, veins dilated over front of chest and diminished movement of right side of Chest; absolute dullness over right upper lung front and back. Breath sounds absent over right upper lobe, poor over lower with occasional rhonchi. Liver enlarged $1\frac{1}{2}$ inches below costal margin and tender. Apex beat in 5th interspace one inch outside nipple.

30.5.31. Gland removed from left axilla.

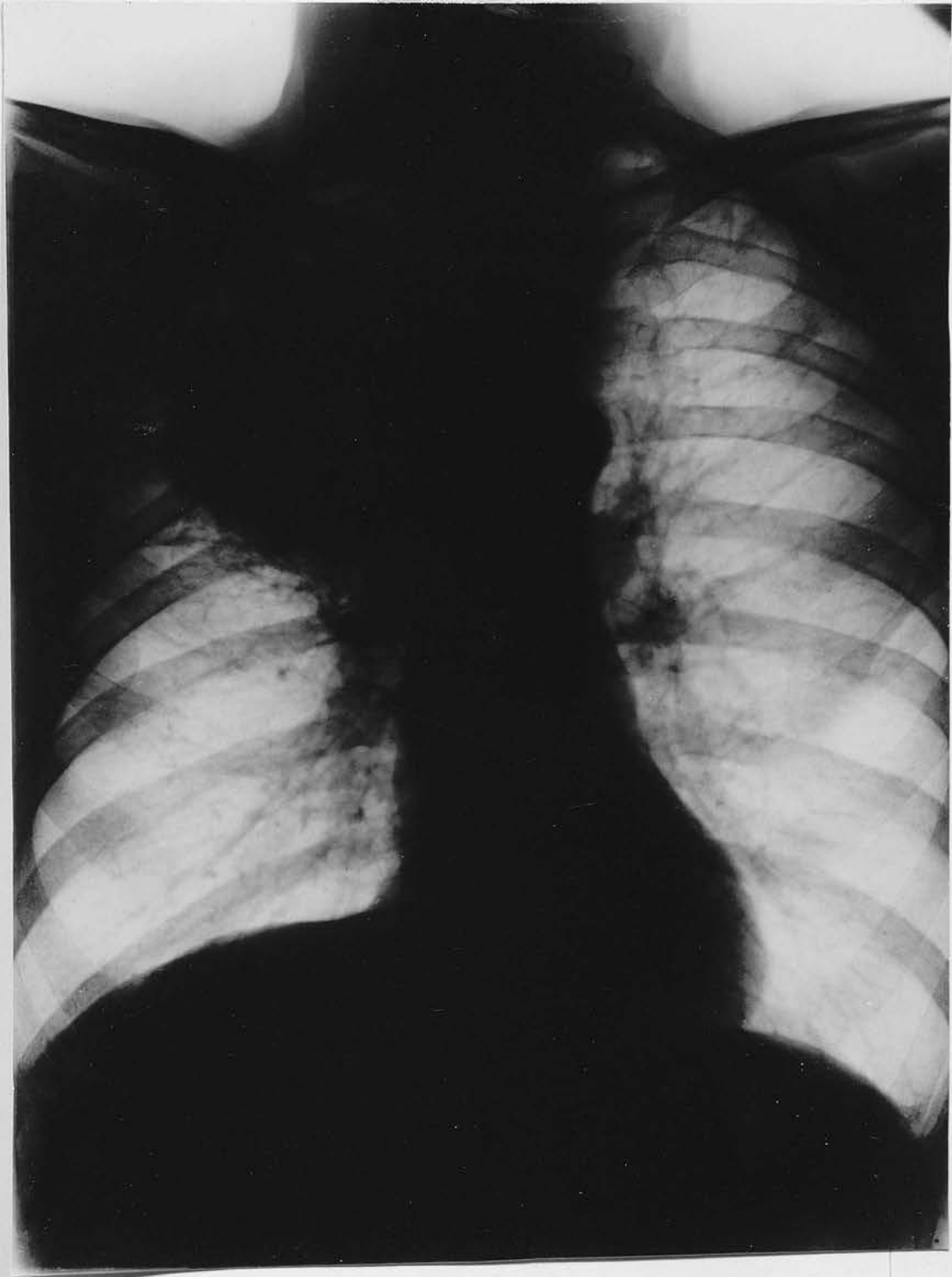
Pathological Report - Sub-acute inflammation. No indication of Carcinoma. Sputum negative for Tubercle bacilli on five occasions.

Wassermann negative.

1. 6.31. Sputum - Pus cells and mononuclears numerous. A few columnar cells from bronchi: no blood. No Carcinoma cells.

2.6.31. X-ray Report. Heart normal. Right diaphragm fixed. Right Lung Carcinoma, right upper lobe.

Fig. III.



8. 6.31. 1 c.c. Lead Selenide given intravenously followed by severe reaction, and signs of Heart failure - Adrenalin and Morphia given.
- 28.6.31. Pain and numbness of right shoulder, face somewhat swollen, slight cyanosis..
- 30.6.31. Swelling and cyanosis greatly increased with very severe dyspnoea and patient died.

Post-Mortem.

Bronchi both contain pus; no obstruction in main bronchi, a branch of the right upper bronchus runs into a neoplasm. Right lung: upper lobe contains a round tumour the size of a cricket ball, sharply defined, white in colour and of soft consistency, the lower edge infiltrating the lung tissue gradually. No other deposits found in the lungs; the apex showed scarring and emphysema. Microscopically the tumour was mainly composed of polymorphic cells, columnar in origin and glandular in nature. The cells ranged from long spindle, columnar and spheroidal cells in solid masses to well-formed acini-secreting mucus. No metastases found.

Case 3.

R.W. Male age 51. Lighterman. Admitted Royal Chest Hospital on 6.11.1929.

Previous illnesses - Haemoptysis fifteen years ago, and at intervals up to two months

ago; Pleurisy six months ago. Cough over two years. At present complains of cough with slight sputum, loss of weight, pain and dyspnoea of five months duration, hoarse voice in last month getting worse, occasional night sweats. Appetite good, bowels regular.

On Examination.

Temperature 99.4° Pulse 80. Respiration 27. Sallow, thin appearance; some clubbing of fingers, tongue clean, teeth and gums in bad condition. Chest of normal shape, poor but apparently equal movement. Vocal fremitus diminished, and dull note at left base, extending as far as spine of the Scapula, breath sounds absent in this area. Rhonchi above this area and at the right base.

Apex beat diffuse in 5th interspace, half inch outside nipple. Blood pressure 105/60.

4.12.29. Cough troublesome, some pain on left side. Slight haemoptysis - dullness on left increasing.

23.12.29. Small amount of pus aspirated from left base - showed Streptococci. Sputum negative on three occasions, with Antiformin method few Tubercle bacilli present. Wassermann negative. No malignant cells in Sputum, numerous red corpuscles.

20.12.29. Small gland dissected from right side of back, on section deposits of Carcinoma cells mostly spindle-shaped, but much variation with some attempt at both columnar and pavement epithelium; primary focus probably lung.

Blood Count: Reds 4016.000
Whites 20.000
H.B. 65%

differential Polymorphs 88%
Lymphocytes 9%
Large Mononuclears 2%
Esinophils 1%

24.12.29. Dyspnoea very severe. 3 ij pus aspirated.

25.12.29. Died.

Post-Mortem.

Left pleura adherent to nearly the whole surface of the lung, thick and collection of pus at the base.

Lung. Left lower lobe fibrotic in its upper part, the rest of the lung collapsed with bronchiectatic cavities. Left lower main bronchus has a growth inside it partially obstructing the lumen. Metastases found in Liver and left Suprarenal.

Section. Typical bronchial Carcinoma of polygonal cell type with Squamous metaplasia; there is

much variation in the cells, some are of the basal cell type, others range from spindle and columnar to round. The mucus glands are replaced by tumour islets in which the cells are undifferentiated masses as in a scirrhus.

Case 4.

A.D. Age 50. Marine engineer. Admitted Royal Chest Hospital 23. 5. 1931.

History. Cough for the last year night and day, Small amount of sputum on occasions blood-stained, Breathless on exertion, lost 3 St. in weight in last year; on one occasion had a sharp pain in left side; pain in left shoulder for last month. Previous illness - only Malaria.

Family. Father died of cancer, Mother has Chronic Bronchitis.

Examination. Thin, wasted appearance, fingers clubbed, many small, hard and fixed glands in left supra-clavicular area. No teeth, large red swelling on lower jaw; tongue dirty. Liver 2 inches below costal margin.

Chest. Left pectoralis muscles wasted. Very poor movement on this side. Vocal fremitus diminished at left apex, absent over middle and lower left lung; percussion boxy in the flank. Breath sounds very poor over front on left side, absent in the flank, many rhonchi with a few coarse rales. Breath sounds also faint on right side.

24.5.31. Gland removed from Supra-clavicular region.

1.6.31. Patient worse. Cough with constant blood-stained sputum, swelling in lower jaw appears to be enlarging; severe pain over praecordium.

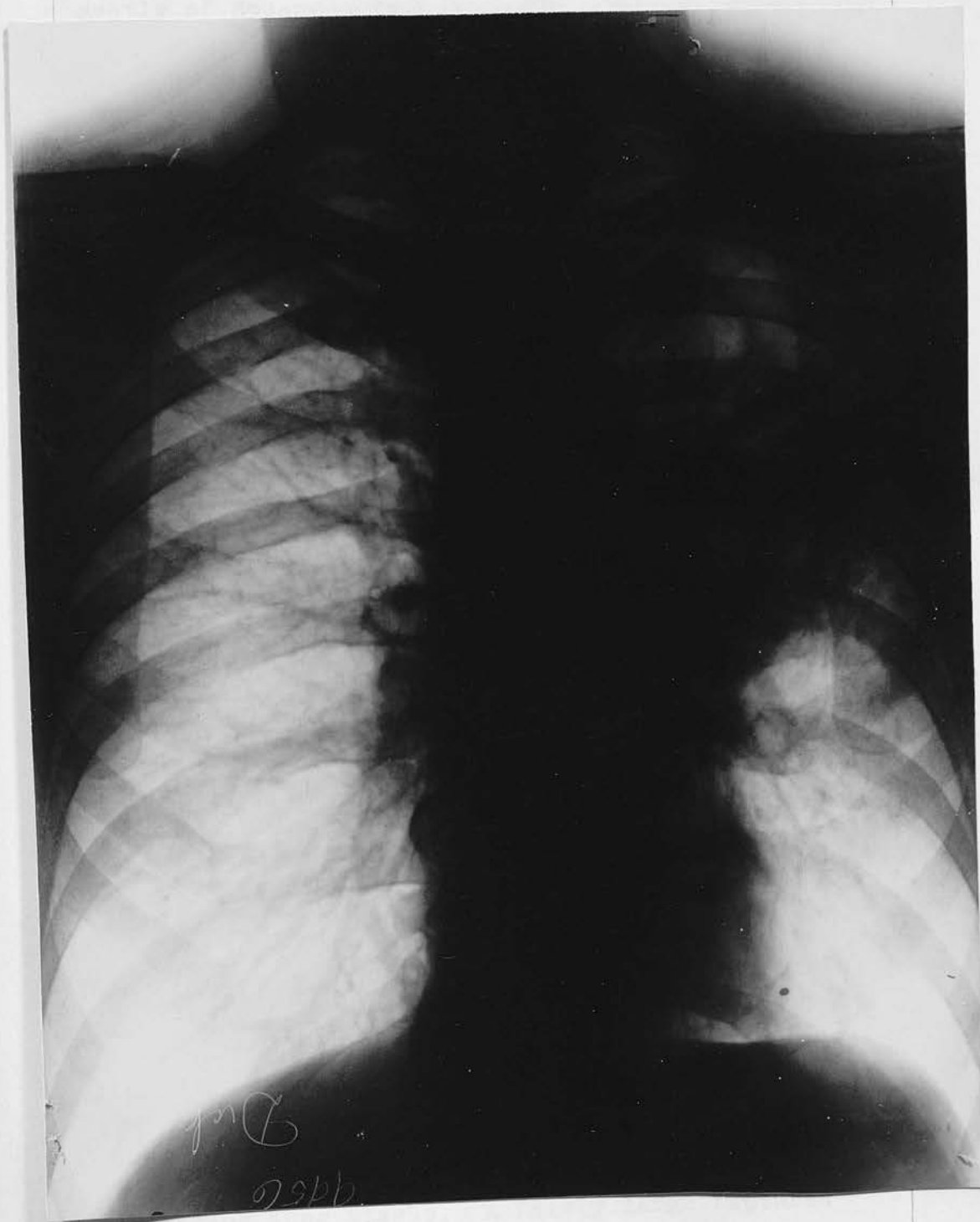
9.6.31. Fatal haemoptysis. Evening temperature varied from 99.6 to 101.2° f.

Pathological Reports. Sputum negative for Tubercle bacilli on four occasions, brownish muco-purulent blood present. Clumps of Squamous type cells, some

with two or three nuclei - unusual in appearance,
pyknotic nuclei common - possibly malignant.

Urine. Albumin trace, hyaline and granular casts, no
pus, few red blood cells. Urea concentration
test - after 1 hour 1.2%, after 2 hours 1.55%.

Fig. V.



X-ray Report. Left diaphragm very sluggish, left upper lobe and left hilar area has opacity very suggestive of neoplasm. (See Fig.V)

Excised Gland Full of Carcinomatous cells, mostly of Squamous type with an alveolar arrangement.
Post-Mortem.

There is a firm white tumour in lower jaw ulcerated with clean raised edges, no fungation; it does not grow from the bone, though its edges are connected with soft, bony tissue. Glands above both clavicles enlarged, left pleura thickened with adhesions to 2nd and 3rd ribs.

Bronchi. A neoplastic nodule projects into main right bronchus just beyond the bifurcation, causing partial obstruction. On the left there is an extensive growth in the wall of the bronchus, ulcerating into the mucous membrane - it extends directly along the bronchus in the upper branch, causing some narrowing.

Lungs. No Carcinoma in right lung; in lower portion there is generalised bronchiolectasis and numerous minute abscesses - No evidence of Tuberculosis.

Left lung has three lobes; in the upper lobe the Carcinoma surrounds the bronchus and spreads along it into the lung; in the middle it opens into a cavity, containing only blood clot, - the walls of this cavity are irregular, nodular and soft, and composed of carcinomatous lung tissue. A fairly large ruptured

vessel projects into it. In the lower lobe there is an extension of the Carcinoma along the bronchi in the hilum; it is partially collapsed with mild bronchiectasis.

Stomach full of blood clot. A nodule of growth on wall of greater curvature.

Intestines. Ulcer in the caecum appears carcinomatous.

Liver. Many small metastases.

Section. Polymorphic-celled Carcinoma, mainly of squamous type.

Case 5.

J.H.H. Age 52 years. Male. Book-keeper.
Re-admitted 27.5.1931.

History. No illness except a "nervous breakdown" four years ago. In September 1930 was seized with a sudden, sharp, stabbing pain in right side of the Chest, with slight feverishness and cough. A fortnight later sputum was blood-stained and breathing difficult owing to pain. He was first admitted to the Royal Chest Hospital on the 13:10:1930, having lost 2 Stone in weight in previous two months. He was discharged on 8:11:1930 with a diagnosis of fibrosis right upper lobe, enlarged paratracheal glands - Neoplasm ? After a fortnight's convalescence he resumed work, attending during this time at the Royal Northern Hos-

pital for Deep X-ray therapy, up to the time of his re-admission.

Examination.

Patient thin and pale with cyanosed lips and ears. Temperature 98.8° P. 88 Resp. 26.

Pupils equal and react to light and accommodation.

Chest. Muscles wasted. Superficial veins enlarged, very poor movement, percussion dullness in upper zone of right lung anteriorly and posteriorly. Breath sounds absent in this zone. Good in middle and lower parts.

No Cardiac displacement.

30.5.31. Complains of severe headache, and praecordial pain. Dyspnoea getting worse, and Cough very troublesome and husky.

9.6.31. Dyspnoea now very bad. Cough prevents sleep. Cyanosis marked.

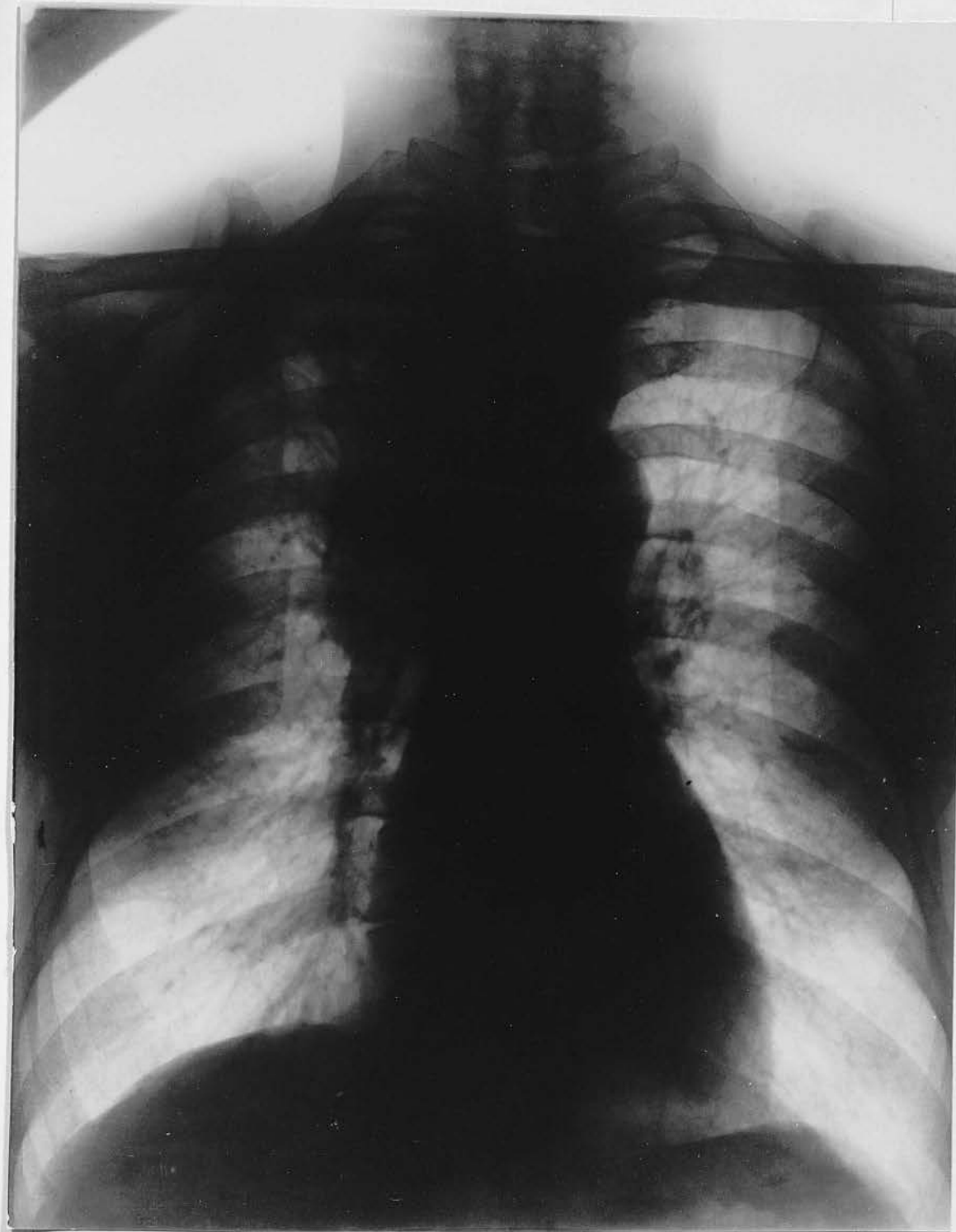
11.6.31. Consulting Laryngologist advised immediate tracheotomy as both vocal chords were fixed in Abducted position. The patient died during the operation.

Pathological Reports.

Sputum negative for tubercle bacilli on three occasions.

No cells of carcinomatous nature found.

Fig. VI.



X-ray Report. Right diaphragm shows paradoxical movement. Neoplasm in right apex and infra-clavicular region. Mediastinal and paratracheal glands enlarged.

Wassermann negative.

Post-mortem.

Pleura opaque with minute white studs on it, adherent at apex and lateral side of right upper lobe, also laterally at left upper lobe.

Mediastinum. The main mass of growth is in the middle and posterior mediastinum; it surrounds the arch of the Aorta, and left Recurrent laryngeal nerve can be traced into it. There is an extension upwards to the right subclavian artery and along the paratracheal glands on both sides; the glands at, and the bifurcation of the trachea are infiltrated and surrounded, and it is continuous into the walls of both main bronchi, causing partial obstruction in both. Some of the glands appear to have caseous foci. The growth was white in colour and of a hard consistency.

Right Lung. Upper bronchus completely blocked by neoplasm which runs into the lung for a short way; main bronchus partially blocked, the lower is free. Bronchiectasis general in upper lobe in smaller bronchi. In the middle lobe is an abscess cavity with a surrounding area of Broncho-Pneumonia.

Left Lung. Apart from growth in the main bronchus, this lung is free from infiltration.

Right Jugular Vein contains a thrombus two inches long.

Abdomen. Neoplastic mass the size of a large plum in the omentum, and a smaller one in the mesentery. Small metastasis in the Pancreas.

Sections.

One cervical gland appears to be a caseous Tubercular one.

Pancreas and omentum show carcinomatous cells.

Tumour is of the small, oval cell type; some are elongated, though there was no definite epithelial structure, a section from near the edge shows a few cylindrical-shaped cells. It has the typical appearance of the oval or oat-celled Carcinoma.

Case 6. A.B. Age 42 years. Lamplighter. Admitted 19.10.1929.

History. Rheumatic fever in 1912. Since then quite well until five weeks ago when he was seized one night with a sudden, intense pain in his left side with severe dyspnoea on the slightest exertion. The pain though less severe has persisted and though it sometimes shifts to the right side it always comes back to the original site. Cough began with

this attack and has persisted since; it is paroxysmal and hacking without sputum. Appetite bad and has Dyspepsia after most meals. Vomited yesterday for first; lost 10 lbs. in weight in the last year.

Examination. General condition good and looks healthy; no wasting; no finger clubbing; no hoarseness.

Lungs. Diminished movement left upper zone with scarcely any movement in middle and lower areas. Vocal fremitus practically absent, percussion note dull; breath sounds faint to absent upper area; in middle zone Bronchophony, in lower area absent; posteriorly in upper area distant amphoric sounds with faint rales.

One small movable gland just above left clavicle in mid-line.

Pupils equal and react to light and accommodation.

- | | |
|----------|--|
| 22.10.29 | 20 c.c. Slightly blood-stained effusion aspirated. |
| 23.10.29 | 45 oz. aspirated and replaced by 400 c.c. of air. After this left chest was resonant down to just below the angle of the Scapula, breath sounds distant and vocal resonance clearer. |
| 24,10.29 | Cardiac dullness gone; breath sounds heard over praecordium with metallic tinkling. |
| 1.11. 29 | Patient feels better and cough improved, but dullness creeping up again in left chest. |
| 8.11. 29 | Few c.c. of thick pus aspirated. Cyanosis becoming marked, tightness in chest; Dysphagia for solids. |

20.11.29 Dyspnoea getting worse, also pain marked,
2 oz. pus aspirated.

Died on 25.11.29. Temperature varied
between 99-101° in first week; after that
normal or subnormal.

Pathological Reports.

Blood Count	Reds	4,480.000	Polymorphs	67%
	Whites	10.800	Lymphocytes	...	21%
			Large Mononuclears		12%

T.B. Negative in sputum and pleuritic fluid.

Pleuritic Fluid - cloudy and bloody, reaction alkaline. Albumin same as blood serum.

Cells. Great many pleural endothelial cells, some binucleate and a few multinucleate. Pus cells and Lymphocytes in equal numbers. Picture of hyperplastic pleurisy and suggests possibility of Endothelioma.

Wassermann negative. Complement fixation with Hydatid Antigen negative.

X-Ray Report, 24.10.29. Left artificial pneumothorax. Good collapse of upper lobe, lower lobe covered with effusion.

Post-Mortem Report.

At the bifurcation of the trachea a growth is present, external to the left main bronchus, small nodules can be seen pressing up under the mucosa. About one inch down the whole bronchus becomes obstructed by a mass of firm, white neoplasm.

Pleura - right normal; on left side one pint of yellowish fluid, firm adhesions posteriorly and thickened, more recent ones anteriorly and laterally - the lobes are adherent and on separation the growth is

seen to have just reached the surface of the lung. Left lung is completely collapsed, there is a massive growth at the root extending along the bronchi into both lobes but mostly into upper. Extensive bronchiectasis especially at the base, many of these cavities containing pus. The large vessels are surrounded by the growth. The Mediastinum is filled with growth, supraclavicular glands show infiltration. Metastases many nodules in the Liver and in glands along the lesser curvature of Stomach.

Section. Main tumour of small oval or "oat" and round cells in alveolar masses; in the liver the structure is more carcinomatous in appearance with epithelial cells and attempts at acini. Points of note in this Case are the acute onset with previous good health, the healthy appearance of the patient with an advanced carcinoma present, the absence of pressure symptoms, except perhaps Cyanosis and the Dysphagia near the end, with marked infiltration of the Mediastinum.

Case 7. D.W. Female. Age 80 years. Admitted to Royal Chest Hospital on 20.10.1930.

History. Always healthy except Rheumatic fever in childhood - one sister died of Haemoptysis aged 29. Complains of haemoptysis since August of this year, occurring periodically though slight. A little cough; sharp pain during last week in right upper chest on coughing or deep breathing. Lost a little weight lately and appetite is bad since illness. Dyspnoea has curtailed walking lately; no hoarseness or dysphagia.

Examination. Looks well for her age, no finger clubbing. Heart not displaced.

Lungs. Expansion poor, percussion note impaired at right middle zone, breath sounds weaker on right side.

Fig. VII.



- 25.11.30 Pain in right shoulder, haemoptysis 2 oz., very constipated, some fever and pulse becoming irregular in force and rhythm. The percussion note in right upper lung is flat and bronchial breathing present; in middle and lower areas are coarse rales, area of poor air entry posteriorly.
- 2.12.30. Cough very troublesome, pain and frequency of micturition - a sloughing urethral prolapse found.
2. 2.1931. Died with very sudden dyspnoea and Heart failure.

Pathological Reports.

Sputum Negative for Tubercle bacilli on five occasions.

Wassermann negative.

Urine. Albumin trace, moderate number of pus cells and bladder epithelial cells.

X-ray Report. 25.10.1930. (See Fig.VII.)

Diaphragmatic movement poor on right. Mass situated in right, middle lobe, with appearance strongly suggestive of Carcinoma.

Fig. VIII.

X-ray Report 17.1.1931.

Heart displaced to right side, right diaphragm fixed. Collapse of right upper lobe and partial collapse of middle lobe which is bronchiectatic. Lower lobe collapsed; appearance suggests bronchial Carcinoma.

Post Mortem Report.

Small growth in right upper bronchus causing obstruction, also a growth in the bronchial wall at the bifurcation, causing some elevation but no obstruction. Lymphatic glands in Mediastinum invaded but not much enlarged. Right pleural Cavity contained about one pint of pale yellow fluid - pleura thick and adherent in patches. Right Lung - Upper lobe solidly infiltrated with neoplasm giving a pneumonic appearance, lower lobe collapsed but no growth. Left Lung - no growth; emphysema at apex and a few pleural adhesions. Liver - one umbilicated nodule found.

Section. Typical bronchial carcinoma composed of very polymorphic cells with alveolar or papilliferous arrangement; some spaces lined by cells columnar and spindle shaped to polygonal and squamous. A few hyaline whorls are seen in the primary tumour, and in the secondary deposits these are very numerous and resemble Hassels corpuscles of the Thymus.

Case 8. H.B. Age 59 years. Painter. Admitted 20.1.1930.

History. For last three months a hard, dry and hacking cough with white, frothy sputum; dyspnoea on exertion; six weeks ago had a sudden paroxysm of coughing bringing on a sharp pain in left side lasting ten days. During the last week noticed swelling of the feet, improving after being in

bed, but never completely subsiding; also some swelling of Abdomen. Not noticed any loss of weight: appetite good; no indigestion; bowels regular. Only previous illness Bronchitis six months ago.

Examination.

Cachectic appearance; pupils equal and react to light and accommodation. Heart not displaced.

Chest: Left side flattened front and back, poor movement. Percussion note impaired anteriorly, dull in posterior middle and lower areas. Weak air entry anteriorly; poor air entry posteriorly and absent breath sounds at base, with corresponding diminished and absent vocal resonance.

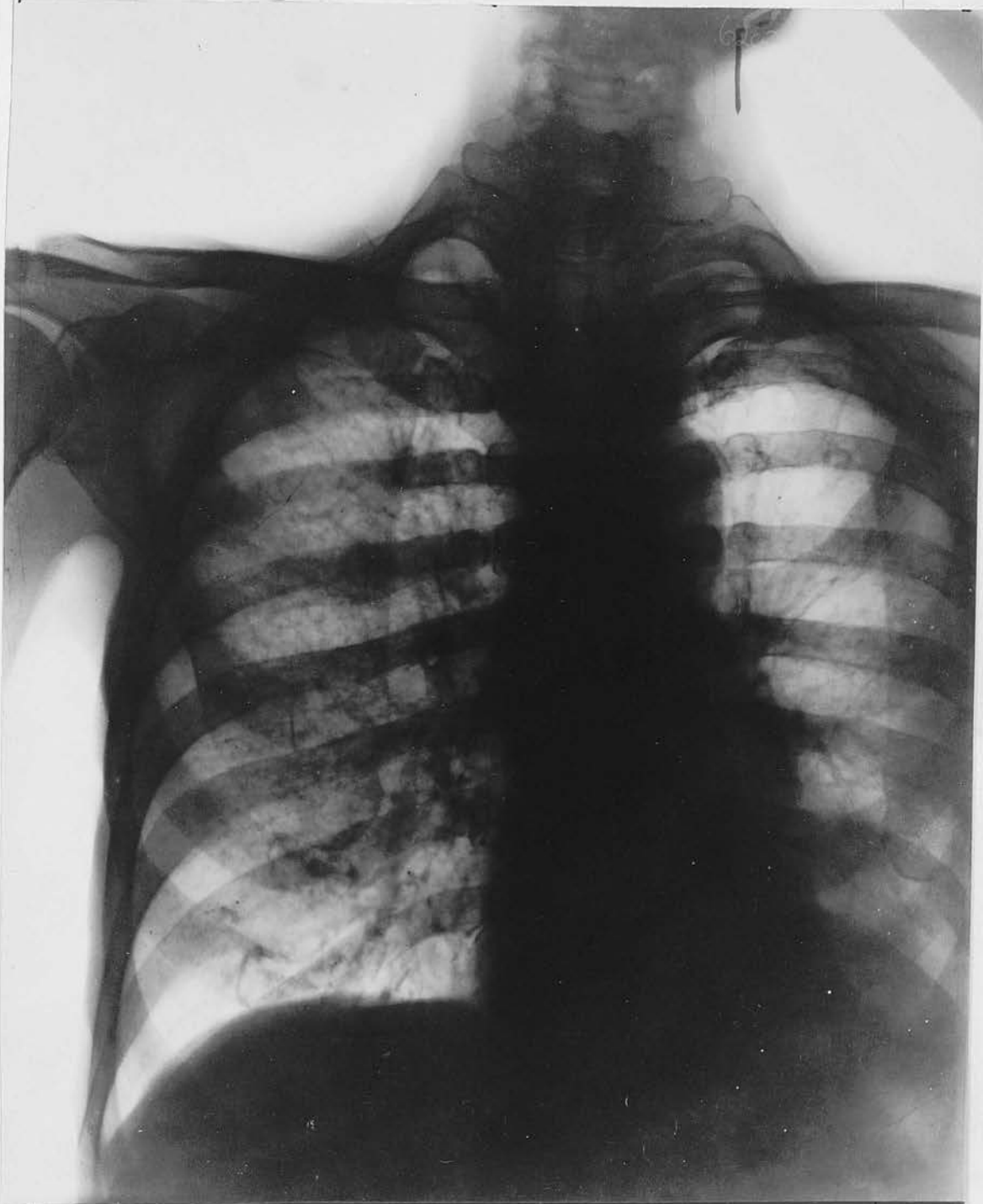
23.1.30 108 oz. clear yellow ascitic fluid withdrawn and Liver not found enlarged.

4.2.30 Cough improved; slight gain in weight, ascites not reappearing.
Vocal chords move equally.

6.2.30 No fluid found at base of left lung on exploration; no breath sounds at base, but in middle area posteriorly few coarse rales, and still higher between Scapula and Spine amphoric breathing.

11.2.30 Appetite poor; much weaker and drowsy.

Fig. IX.



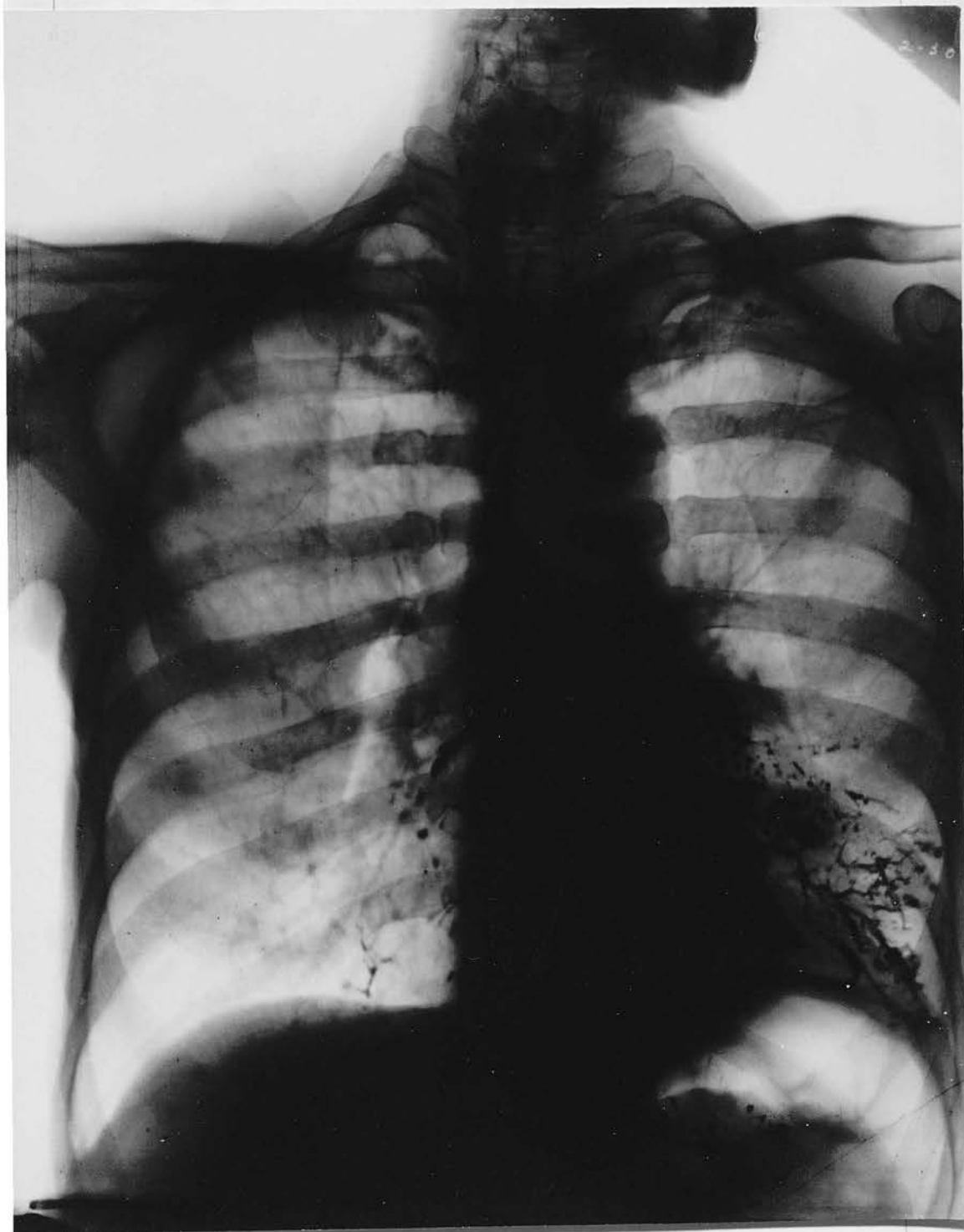
24.1.30 X-ray Report. Heart normal. Lower lobe on left side collapsed with some slight effusion.

13.2.30 Patient suddenly collapsed and died.

Pathological Reports.

Wassermann negative. Sputum negative for bacilli on three occasions. Pus cells found. No malignant cells. Organisms scanty, chiefly pneumococci. Ascitic fluid Many polymorphs, and numerous multinucleate cells suggestive of Carcinoma. No organisms found.

Fig. X.



4.2.30 X-ray after Lipiodol injection.

On screening immediately after, the left lower bronchus appeared completely obstructed: Fig.X was then taken, though in this a little lipiodol appears to have trickled through. Fig.XI, a lateral view, shows a similar condition.

Fig. XI.



Post-Mortem Report.

Left Bronchus. About one inch from the bifurcation is a neoplasm in the bronchial wall filling up the lumen; it extends tongue-like up the lumen as far as the bifurcation, obstructing also the branch to the upper lobe. The total extent of the growth in the wall does not exceed a half-inch band; it is white and firm. The glands in the immediate neighbourhood are not visibly infiltrated; immediately beyond the growth the bronchus is dilated and filled with blood-stained pus. The lower lobe appears consolidated and very hard and apparently there is some extension of the growth into it; no cavities are present. Right lung contains numerous small shotty nodules. Hilar and Mediastinal glands show no abnormality. Abdomen contained half a pint of clear fluid. Splenic flexure and gall bladder bound down by adhesions. Liver - Some perihepatitis with small nodule of growth on under-surface. Some fibrosis round portal system.

Section of growth in left lung showed the tumour situated chiefly under the epithelium and spreading amongst the bronchial glands; it is composed of spheroidal cells with little cytoplasm or construction. The base shows bronchiectasis and chronic inflammation between small abscesses; the interstitial tissue is much increased and there is endarteritis.

Right Lung. The shotty nodules are carbon dust with fibrosis. Nothing to suggest Tuberculosis. A gland taken at random from the side of the trachea contained carcinoma cells arranged as in a Scirrhus.

Liver. The cells in this metastasis are better formed cubical or columnar arranged in rows along trabeculae.

Case 9.

W.D. Age 54 years. Army pensioner. Admitted Royal Chest Hospital 20.8.1930.

History. Bronchitis while in the Army in 1915; invalided out in 1918 with Chronic Bronchitis. Cough always bad since then, with moderate amount of white, frothy sputum. Moderate health until May 1930 when he had severe Influenza. The sputum from now increased in amount with dyspnoea and loss of weight. In June 1930 blood was seen in the sputum on frequent occasions. He was now constantly tired and shortness of breath was constant.

On Admission. Cough very severe, loud and distressing, sputum muco-purulent. slight pain in right chest posteriorly; dyspnoea fairly severe, appetite poor; Bowels regular, no indigestion.

Examination.

An ill-looking, cachectic man with constant cough and dyspnoea, cyanosis of lips, pupils equal and react to light and accommodation. Mouth edentulous, gums healthy, tongue dirty with whitish fur, breath foetid.

No palpable glands. Chest: Muscles very wasted, some flattening on right side; percussion note impaired below right clavicle with diminished air entry and very weak breath sounds; Amphoric breathing in small area. At base dry rhonchi. In the Left Lung signs of Chronic Bronchitis and emphysema.

Fig. XII.



X-ray Report. 23.8.1930. Trachea over to right side. Heart displaced to right side. Collapse of right lower lobe? Upper lobe infiltrated, with a cavity showing just under clavicle. Left Lung emphysema.

Sputum Negative for Tubercle on two occasions.

Wassermann negative. Temp. varies from 98.4 to 101.8°
Pulse 86 to 110. Respiration 23-30.

- 2.9.30. Bronchoscopic Examination. Right bronchus contains much pus, granulomatous mass seen in this bronchus about one inch beyond bifurcation; bleeds readily. Specimen removed for examination.

Fig. XIII.



- 6.9.30. X-ray after Lipiodol. No obstruction of right lower bronchus, there is general fusiform bronchiectasis; trachea somewhat kinked just above bifurcation.

Section of bronchoscopic specimen - Typical
bronchial Carcinoma of columnar and flattened cells.

- 10.9.30 Patient steadily going downhill; haemoptysis more frequent and severe, often 3 to 4 oz. daily. Dyspnoea severe.
- 20.9.30 Temp. 102.4° Sputum now offensive; percussion note dull at right base with absent breath sounds. Moist rales over practically the whole lung.

Died 25.9.30.

Post-mortem.

Oesophagus, pericardium and left pleural cavity normal. Right pleural cavity obliterated by adhesions, so firm that some portions of the lung came away with stripping, especially at the apex.

Right Lung: There is a neoplasm in the upper lobe arising from the right upper bronchus about three-quarter inch from its commencement. This lobe was almost gangrenous in places with an offensive odour, there was a small cavity. The lower lobe was consolidated. There were glands infiltrated in the post-mediastinum, and two glands at the bifurcation of the trachea also infiltrated.

Heart - dilated, muscle pale and brown.

Left Kidney. Hydronephrosis of pelvic type with very little renal tissue left, at junction of ureter and pelvis was an aberrant renal artery.

Right Kidney enlarged but otherwise normal.

Section.

Carcinoma with much metaplasia, evidently of bronchial origin, consisting of cells resembling stratified epithelium; in other parts they were more of an adeno-carcinomatous nature. No cell nests were found.

Case 10.

R.W. Age 54 years. Admitted 5.11.1930.

History. Never had any serious illness though for some years past suffered from piles and indigestion and flatulence. In June 1930 a cough started and there was dyspnoea on moderate exertion; never had haemoptysis or haematemesis. Sputum very slight, white and frothy. Indigestion lately worse.

Examination.

Patient pale, sickly-looking woman with an anxious expression; no apparent dyspnoea; tongue fur-red, pupils equal and active to light and accommodation.

Chest: Poorly covered and movement diminished.

Apex beat in 6th interspace one inch outside mid clavicular line, forcible impulse. Cardiac dullness spreads upwards and to the right. Second sound in mitral area accentuated and reduplicated; second pulmonary accentuated, in Aortic, both sounds loud, no murmurs, no thrill, no tracheal tug. Blood pressure 160/98.

Lungs. Percussion note dull in infra clavicular area both on left and right for about two inches

on either side of manubrium; breath sounds in this area faint or inaudible; posteriorly on left side bronchial breathing in area between spine and Scapula; near base coarse friction sounds - percussion note impaired all over. On right side few moist rales.

Pulse. Radial and brachial arteries thickened and somewhat inelastic, regular and good volume, right pulse six beats more per minute than left.

Abdomen. Tenderness in epigastrium. Reflexes normal.

- 14.11.30 Patient steadily more dyspnoeic, has to be propped up. Sharp pain on left side, between 6th and 8th interspaces in mid-axillary line - friction rub.
- 16.11.30 There is a suggestion of fluid at left base but patient refused exploration.
- 3.12.30 Severe attacks of paroxysmal dyspnoea, "feels Chest full of sputum but cannot expectorate." Bubbling rales all over Chest.
Died 4.12.1930.

Pathological Reports. Wassermann negative.

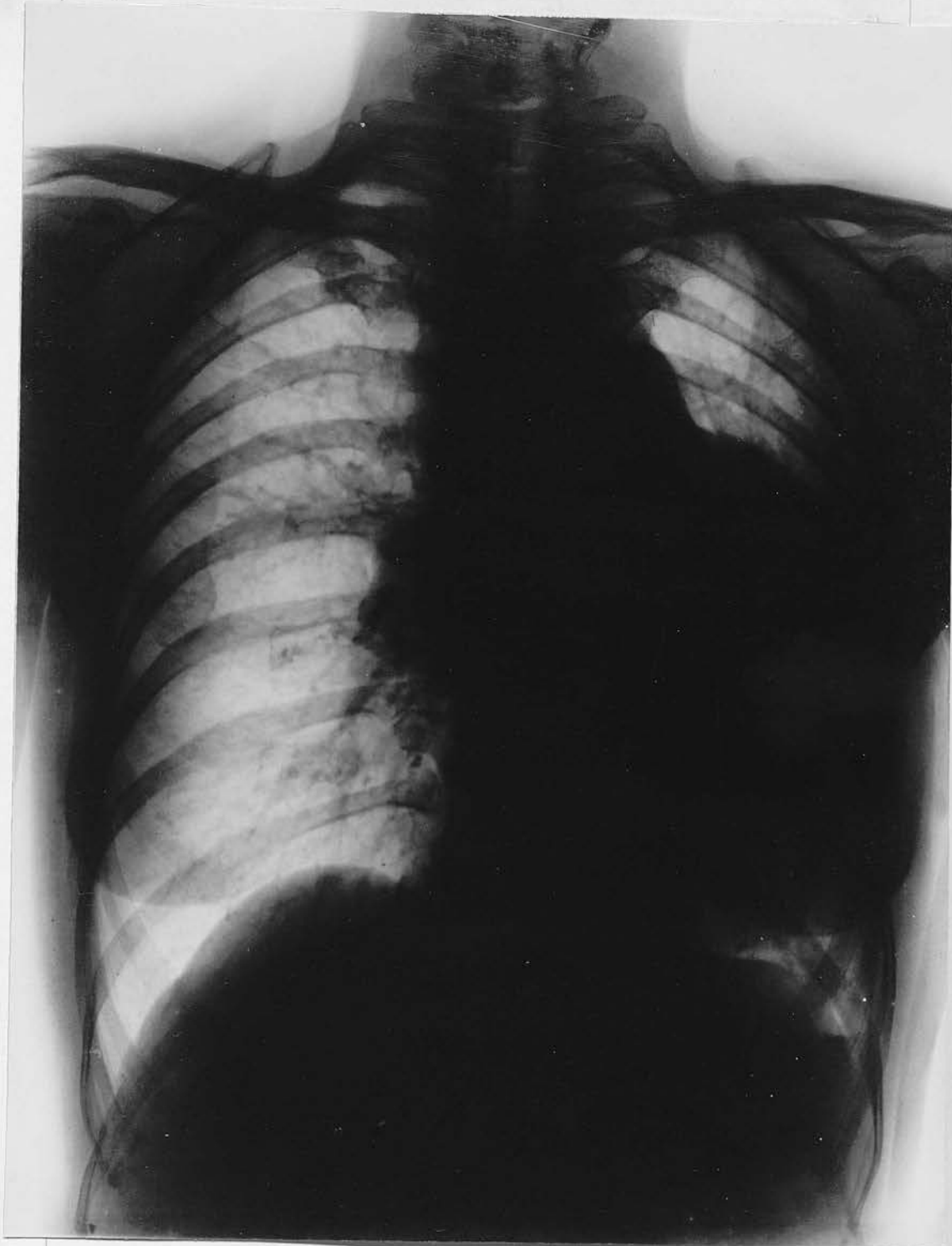
Sputum negative for Tubercle on two occasions.

12.11.30 Blood urea 27 mgms. %

22.11.30 Count White blood cells 18,600,
Polymorphs 90%

Urine: few pus cells. No red corpuscles or casts.
On culture a few colonies of B. Coli.

Fig. XIV.



X-ray Report. Heart displaced to left side; Aorta atheromatous and dilated.

9.11.1930. Appearance suggests Aneurysm compressing left bronchus.

Post-mortem.

A small nodular growth in Thyroid. Pleura adherent over nearly whole of left lung, no fluid. A few pleuritic adhesions over right lung.

Right Lung: Slight obstruction by nodular projections, with some ulceration, in main bronchus. In the upper lobe is a thrombosed vessel with large infarct. No neoplasm in body of this lung.

Left Lung. Main Bronchus considerably obstructed by projecting nodules. Upper lobe emphysematous, the growth is round the bronchus and infiltration is downwards along the vessels as a soft, white mass into the lower lobe; this lobe is solid with diffuse Carcinoma and Pneumonia; pus oozes out of numerous dilated bronchioles and there is much collapse.

Mediastinum: Nodular mass of infiltrated glands in the superior and middle.

Heart - Normal in size, muscles soft, valves normal.

Some pouching of ascending aorta and one patch of Atheroma.

Abdomen: Glands at lesser curvature of Stomach and round the portal vein infiltrated with growth. Two nodules of growth in the Liver.

Sections. Typical small-celled Bronchial Carcinoma with round and oval cells in masses without any sign of tissue structure, with fibrillar bands of connective tissue. The thyroid metastasis infiltrated between and within the vesicles.

This case presented some interesting diagnostic difficulties, the signs and symptoms would have been possible with either Neoplasm or Aneurysm. The X-ray report favoured Aneurysm, but the negative Wassermann, absence of valvular murmurs and booming second aortic sound were against it. The polymorph leucocytosis and Pleurisy again favoured Neoplasm.

SUMMARY AND CONCLUSIONS.

- I. From a "thorough" study of the literature, and from my own clinical experience, the incidence of Primary Bronchial Carcinoma is markedly and definitely on the increase.
- II. Though no definite etiological factor is found responsible for this disease or for the increased incidence, the conclusion is drawn that some irritants of unknown origin acting on the Bronchial Mucosa play some part, and that these irritants are now in greater concentration in the atmosphere than formerly.
- III. The only known instance where Primary Bronchial Carcinoma occurs as an occupational disease is in the miners of the Schneeberg. This is due to the presence of certain unknown irritants peculiar to these mines. A historical survey shows that the occurrence, though not the nature, of this disease was known from medieval times.
- IV. The pathology is fully described and classified and arguments advanced in favour of the new conception of Barnard, and in explanation of the origin of the different types of tumours.
- V. There are no pathognomonic symptoms or physical signs, but there are certain symptoms and signs which

which should arouse suspicion of the presence of Primary Bronchial Carcinoma. All the symptoms and signs are analysed according to their frequency and importance in the series of fifty nine cases, and the pathological conditions giving rise to them are mentioned.

VI. The accessory methods of examination are described and their indications, importance, and relative merits emphasised.

VII. A short account of modern methods of treatment is given, and finally ten clinical Cases are described, including their X-ray appearances and post-mortem reports.

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